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PRECAUTIONS IN USE OF ANTIHYPERTENSIVE DRUGS, INCLUDING CHLOROTHIAZIDE

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The aim in antihypertensive therapy should be to lower the blood pressure gradually by using the safest, mildest, and least symptom-producing drugs; dosages are determined by patient observation over weeks or months of time. One of the various preparations of Rauwolfia should be used first, an effort being made to achieve the antihypertensive effect without depression. A second drug, Veratrum, may be added if extensive trial has shown the first alone to be inadequate. Again an effort is made to lower the blood pressure without side-effects; in the case of Veratrum these are usually nausea and vomiting, rarely cardiac arrhythmia and collapse. A third drug to be tried with Rauwolfia is hydralazine; it is a potent hypotensive drug, but it can have acute and chronic toxic effects. The fourth is chlorothiazide, which can, in addition to a desirable hypotensive effect, cause diuresis and quickly deplete the body of potassium. The dosage should be kept low and supplements of potassium should be given in patients receiving long-term treatment. A fifth class of available drugs are the ganglionic blocking agents, the dosages of which are so critical that especially exacting care is needed in adapting them to the individual case. Each class of drug may be used in combination with the others, but every change should be instituted gradually. By use of minimal effective doses of drugs in combination, a safe antihypertensive regimen can generally be developed.

Powerful tools can be helpful or dangerous, depending on how they are used. This is particularly true of drugs. An agent that is capable of suddenly altering a vital physiological function such as blood pressure may be either lifesaving or lethal depending on when and how it is given. As more effective hypotensive drugs become available, increasing caution is required in regulating the timing and sizing of their doses, particularly if they are to be used in combination. Conservatism as to the size of doses and the rate of change of doses is one key to success, especially if therapy is to be continued over long periods of time, as usually is required in the management of essential or primary hypertension. This is particularly true in patients past middle age, who do not easily tolerate sudden shifts in their fundamental physiological functions.

Selection of Drugs

Unless there is great urgency for an immediate striking hypotensive effect, as there may be in cases of hypertensive encephalopathy or "malignant" retinopathy, the aim in antihypertensive therapy should be to lower blood pressure gradually through the use of the safest, mildest, and least symptom-producing agents and doses. This obviously requires a process of trial and error in each patient over weeks or months of time. In the usual case of gradually progressive or nonprogressive hypertension there is ample time to undertake such a trial. Although there is a rough correlation between the amount of treatment necessary and the severity of the disease (as indicated by height and "fixation" of the diastolic pressure, the prior duration of the disease, and the extent of vascular complications in the eyegrounds, brain, heart, and kidneys), the proper selection of

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drugs and dosages can be determined only by trying them in a given patient. Therefore therapy is always begun with the mildest drug, Rauwolfia, which may be surprisingly efficacious, even when given alone and in severe cases.

The next drug to be added to Rauwolfia, if necessary, is Veratrum. Veratrum is a powerful hypotensive agent, but it has a built-in limiting or safety feature in its emetic action which serves to protect the individual from lethal doses of the drug given by mouth. After over 10 years experience with this agent, I am confident that it is relatively safe; for even when collapse reactions occur from overdosages, they are rarely if ever fatal. Certainly slow accumulation or chronic toxicity does not occur from Veratrum.

The third drug to be added (or the second if pulse rate is already low on Rauwolfia without Veratrum) is hydralazine. Hydralazine is a potent hypotensive drug, but it can have acute and chronic toxic effects. These may be in the nature of individual idiosyncrasy but are usually related directly to the size of the doses taken. Fourth on the list of hypotensive drugs is chlorothiazide, the new orally effective, synthetic diuretic. This drug has powerful effects on electrolyte excretion and can quickly deplete the body of potassium. Doses necessary for a desirable hypotensive effect over prolonged periods of time can and should be kept low, as compared with those necessary to control edematous states.

The last group of hypotensive drugs to be employed are the ganglionic blocking agents. Dosage is so critical with these drugs that the term "titration" is employed to indicate the exacting care that is necessary in the individual regulation of doses. The purpose of this paper is to point out the precautions to be used in giving each of these drugs, and the unfortunate results that may happen when these precautions are ignored.

Rauwolfia and Reserpine

Details as to various commercial preparations of Rauwolfia and their dosages were given in a recent publication.[1] It was pointed out there that reserpine seems to be the chief active hypotensive principle as well as the chief "tranquilizing" principle in this drug. (Whether these two principles are really separable is open to question.) Because reserpine is used freely in large dosages and with relative safety in psychiatric cases, doctors have been inclined to employ what to me seem unnecessarily large doses in the chronic treatment of hypertension.

While initial dosages of reserpine up to 1 mg. a day may be more rapidly effective in lowering blood pressure (as indeed 5 mg. parenterally may be in cases of encephalopathy) there is little if anything to be gained by continuing such doses beyond a few days. My initial dosage of reserpine in a new ambulatory patient rarely exceeds 0.4 mg. a day (given in four 0.1-mg. doses), whereas the continuing dosage after a few weeks or months of therapy rarely exceeds 0.2 mg., and often is only 0.1 mg. a day. Undoubtedly this low dosage schedule accounts for the rarity with which I have encountered mental depression and for the fact that I have never had a suicide of a patient taking Rauwolfia in any form. However, I believe that my results in hypertension compare favorably with those of physicians who routinely employ doses of Rauwolfia up to 10 times larger than I do.

As just indicated, the duration of continuous treatment with Rauwolfia is most important in determining the amount of the drug that can be safely tolerated. I have had many patients who after even one to two years have had to have their doses of Rauwolfia further reduced, because of the development of intolerable sedation or depression. For example, a few such patients can tolerate no more than 0.1 mg., and an occasional one no more than 0.05 mg., of reserpine a day. As a rule the hypotensive effect can be maintained by giving doses of the drug just below those causing intolerable sedation.

Whether anything is to be gained by using one form or preparation of Rauwolfia in preference to another remains unsettled. Rauwolfia in any form has such a slow gradual action that to sharply assay its clinical effects is most difficult. This applies equally to its hypotensive and to its "tranquilizing" effects. Therefore when one undertakes to make exact comparisons of these two effects among several different preparations of the drug, i. e., to determine their "hypotensive-sedative ratios," one has embarked on an arduous task.

I suspect that my experience with Rauwolfia would be considered "extensive" if the variety as well as the number and duration of my clinical trials were considered. Be that as it may, I have found that in treating hypertensive cases clinically there is little to choose between using crude Rauwolfia, the alseroxylon fraction, or reserpine,[1] provided one employs doses of each low enough to avoid untoward side-effects, particularly depression. In many patients these doses decrease markedly with time and often are as low as 0.1 mg. of reserpine, 2 mg. of alseroxylon, or 50 mg. of crude root a day.

However one practical difficulty still exists, which at first may seem trivial. That has to do with the size of pills that are available. Tablets containing more than 100 mg. of the crude root are not usually made because the bulk of the drug is so large. However it just so happens that this size tablet of crude drug suffices quite well since the drug in this dose is effective when given one to four times a day. As best I can judge, an equivalent dose (hypotensively and sedatively) of reserpine is somewhere near 1/1,000th (by weight) of the effective

dose of the crude root in the same patient. But the usual pills of reserpine contain 0.25 mg. (1/400th the weight of the usual crude pill) and therefore in my opinion would represent considerably more, certainly not less, activity than a 100-mg. tablet of the root. Hence the tendency of the practitioner to overdose with reserpine as compared with crude root.

As for alseroxylon, I estimate that it represents in activity the equivalent of about 50 times the weight of crude root and about 1/20th the weight of reserpine. Fortunately, the manufacturers have made the tablet size of alseroxylon (2 mg.) roughly equivalent to that of the 100-mg. tablet of crude root and definitely less than that of the 0.25-mg. tablet of reserpine. Put another way, a 0.25-mg. tablet of reserpine would be equivalent to at least two tablets of alseroxylon or crude Rauwolfia.

The point is that, because of the sizing of the pills made generally available by the manufacturers, total daily doses of 1 mg. (or more) of reserpine are commonly recommended and used, whereas total daily doses of 20 mg. of alseroxylon, and especially of 1 Gm. of crude Rauwolfia, are rarely if ever suggested for the treatment of hypertension. If my estimations of the relative potencies of these preparations are even approximately correct (and I have good reason to believe they are), I would only expect that reserpine would be blamed (as it is) by clinicians for being more "toxic" than the less purified forms of the drug.

In addition to depression, side-effects of Rauwolfia which may require a reduction in dosage include first of all nasal stuffiness. This appears to be due to vascular congestion of the turbinates, and it may be associated with easy nasal bleeding, or with acute or chronic sinusitis. Vasoconstrictive nasal drops or inhalations often adequately offset this unpleasant side-effect, and occasionally an antihistaminic agent may relieve it. Weight gain frequently, insomnia or diarrhea occasionally, and bradycardia rarely are great enough to necessitate a reduction in dosage of Rauwolfia.

Veratrum

Although pure alkaloids and purified extracts of Veratrum are available, for practical purposes they all have the same objectionable feature as the crude drug, namely that they readily cause nausea and vomiting. From the doctor's point of view this feature may not be undesirable, since it makes overdosing with the drug so unpleasant that patients are not likely to do this very often. Nevertheless, collapse can occur on excessive dosage, and, in association with it, cardiac arrhythmias as well as vomiting may appear. The chief undesirable characteristic of such an overdosage effect is that it may occur with very little increase in the dosage over that necessary to produce a desirable hypotensive effect. Therefore in order to get the maximal beneficial action from Veratrum a patient must be always uncomfortably close to nausea.

These critical dosage characteristics make it necessary to be very precise with the timing of doses during the administration of Veratrum. Patients are advised to take the drug by the clock, e. g., with meals and at bedtime, and never oftener than every four hours. The first dose in the morning (after fasting) may be larger than the noon or supper doses, as may be the bedtime dose (since lying in bed lessens the tendency to nausea or collapse). Thus a common Veratrum schedule, using the alkavervir fraction (Veriloid), is, at breakfast 3 mg.; lunch 1.5 mg.; supper 1.5 mg.; and at bedtime 3 mg.

Given in association with Rauwolfia (e. g., Rauwiloid + Veriloid), even larger doses of Veratrum may be tolerated, as for example, 1 tablet (3 mg.) four times a day, or 1½, 1, 1, 1½ tablets in the four doses respectively. (Incidentally, this latter dosage provides a total of 5 mg. of alseroxylon.) A word as to the use of such combined pills. The purist may rightly object to combination tablets, but patients as a rule greatly prefer taking one tablet to two separate ones. Indeed many apprehensive patients bridle at taking a dosage of two separate tablets at a time, even of the same kind, because they interpret this as meaning that they are more seriously ill. My experience has been that patients have fewer lapses and make fewer mistakes in dosage, the simpler the regimen can be made. Therefore I do not hesitate to use more than one medicament combined in one tablet, provided this gives approximately the correct dosage of each.

The best compromise with Veratrum in any case is for the patient and the physician to become familiar with a single standardized preparation of the drug and gradually to change the dose as necessary to get the best clinical effect with the least nausea. Epigastric, substernal, or pharyngeal burning with salivation often precede nausea and may be useful premonitory symptoms of overdosage. If the patient will lie down at the appearance of these symptoms and omit or reduce the next dose (and then slightly reduce the same dose the next day), he may prevent a recurrence of these overdosage effects.

Hydralazine

Hydralazine is a potent and useful hypotensive drug, but success in its use is dependent mostly upon the manner in which it is given. Indeed, after my first trials with this drug I discarded it because the side-effects seemed too difficult to manage. However by giving preliminary or simultaneous doses of Rauwolfia and by using smaller initial doses of hydralazine, its side-effects were so minimized that my unfavorable opinion was completely altered.

Rauwolfia or reserpine greatly lessens a patient's initial reactivity to hydralazine which usually causes more or less occipital headache and palpitation (possibly due to histamine release). By starting with doses of only 10, or even 5 mg., four times a day and gradually increasing these amounts, one can make the drug tolerable to most patients even in the usual necessary dose of 50 mg. four times a day. However in many patients a total dose of only 100 mg. (25 mg. four times a day) given in combination with reserpine 0.2 or 0.4 mg. a day may suffice to restore the blood pressure to the desired level. The highest dosage of hydralazine I ever use now is 400 mg. a day, and this only upon cautiously demonstrating that it is both well tolerated and efficacious in lowering blood pressure.

Hydralazine, presumably by stimulating cardiac output, can cause angina pectoris in patients with otherwise asymptomatic coronary disease. This manifests itself as substernal aching which is not as clearly related to effort or excitement as in the typical case of angina but often is associated with electrocardiographic changes suggesting myocardial anoxia. While a downward adjustment of the dosage of hydralazine may relieve this side-effect, it would seem preferable to omit the drug altogether in any patient who develops angina while taking it. However it is only fair to say that I know of no deaths from coronary disease in which hydralazine has been clearly implicated.

At the first sign of a hypersensitivity reaction either in the skin, joints, or blood (lupus erythematosus cells, or anemia) hydralazine therapy is stopped. On the relatively low dosages now recommended such complications are rare.

Chlorothiazide

Chlorothiazide, a new orally effective diuretic, is particularly useful as an adjunct with other antihypertensive treatment, whether drugs or splanchnicectomy.[1] The rationale for its use is based on three considerations: 1. Experimentally, almost every procedure that tends to lower blood pressure also tends to cause antidiuresis and sodium retention, which presumably are part of the homeostatic mechanisms that maintain blood pressure.[2] 2. Clinically, hypotensive drugs, particularly Rauwolfia and hydralazine, may cause fluid retention, even to the extent of producing dependent edema. 3. Hypotensive procedures may lose their effectiveness when there is a subclinical, but especially when there is a clinical, retention of sodium and water, particularly with congestive heart failure. Diuresis may then restore the effectiveness of the hypotensive procedure.

Chlorothiazide is tolerated by most patients over long periods of time if given in moderate daily doses. It is a very potent diuretic, being about as effective orally as mercurial preparations are parenterally. It has no serious toxic effects, at least so far as is now known, although a few instances of skin rash have been noted among patients taking this drug. Nevertheless, chlorothiazide can have some untoward side-effects which necessitate caution in its use, particularly when given continuonsly for long periods of time.

A lowering of the serum potassium level occurs in roughly 40% of patients taking chlorothiazide continuously without supplementary potassium for more than a week. In half of these cases the serum potassium level may be reduced below the lower limit of normal (3.5 mEq. per liter). Apparently the body itself in time may correct or lessen the hypokalemia (as it does the hyponatremia) without special dietary supplements of potassium. Restriction of dietary sodium apparently increases the likelihood of hypokalemia, presumably because the kidney will excrete potassium more actively if sodium is not freely available. Therefore patients starting on chlorothiazide should not be placed on a low-sodium diet, and patients already on a low-sodium diet should relax it when chlorothiazide therapy is instituted. Even with this precaution serum potassium level may become so low that it is alarming to the physician and I suspect may be harmful to the patient, especially if he is subject to cardiac arrhythmias as a result of digitalization, coronary ischemia, or both.

For these reasons I never prescribe chlorothiazide for a new patient who may have coronary disease or who is taking digitalis without instituting the chlorothiazide therapy most cautiously and supplementing the intake of potassium as indicated by weekly determinations of the serum potassium level as well as by clinical and electrocardiographic assessments of myocardial irritability and digitalis intoxication. Potassium may be given either in a solution (potassium Triplex) or with specially coated or prepared tablets of potassium chloride. Routinely 14 mEq. of potassium (1 Gm. of potassium chloride) is prescribed in such cases two to four times a day, unless there is renal insufficiency, in which case measurements of the serum potassium level must be utilized to determine the need (if any) for supplemental potassium.

There have been five deaths among several hundred patients who have been given chlorothiazide in this hospital. All these patients were known to have severe generalized vascular disease, had had prior coronary occlusions, or had complained of angina pectoris. Three patients had had a lumbothoracic splanchnicectomy at least 10 years previously. In two of the patients chlorothiazide therapy had been stopped several days prior to death. However, the deaths were "cardiac" in all and were sudden in all but one. Obviously in such critically ill patients sudden death is not unusual and could not be blamed with certainty on the medicament being taken.

Nevertheless it seems possible that there may have been a connection between the use of chlorothiazide and death in some of these cases. This is because in other patients chlorothiazide apparently has precipitated arrhythmias or has caused digitalis intoxication, presumably by producing a diuresis with or without hypokalemia. My present thinking is that patients with areas of myocardial ischemia due to coronary disease (with or without hypotension) may be particularly susceptible to hypokalemia, or to some change in sodium-potassium balance caused by chlorothiazide, which in them may cause a fatal arrhythmia such as ventricular fibrillation.

Chlorothiazide rarely if ever appears to aggravate or cause angina pectoris, as hydralazine may do, in patients with known coronary disease. Indeed it may give striking relief to certain patients with the anginal syndrome, especially if an important component of their discomfort is shortness of breath on exertion. Many anginal patients prefer chlorothiazide to nitrites for prevention of their attacks. For these reasons, when antihypertensive treatment in addition to Rauwolfia and Veratrum appears to be urgently needed in a patient with known or suspected coronary disease, with or without angina pectoris, I am inclined to try chlorothiazide before using hydralazine. However, all the precautions already mentioned in connection with such cases are routinely followed.

As to dosage, chlorothiazide should be given in hypertension in the minimal dose effective in reducing the blood pressure to the desired level. To a large extent this dose will be determined by the treatment being continued at the time of the institution of chlorothiazide. Unless the patient has undergone splanchnicectomy or is taking a ganglionic blocking agent, a starting dose of 125 mg. (½ tablet) twice a day is safe and adequate for initial trial in most patients. However patients with surgically removed or chemically blocked sympathetic nervous systems may be exquisitely sensitive to the hypotensive effect of chlorothiazide and require an extremely cautious approach in their use of this drug. Thus, initially only 62.5 mg. once or twice a day should be given to such patients, and care should be taken to reduce drastically the doses of any ganglionic blocking agent being used, if and as the chlorothiazide is increased. Otherwise severe postural hypotension and collapse may occur.

If, after a week or two at a low-dosage level, blood pressure is still elevated and the serum potassium level is normal (with or without supplementary dietary potassium), the dosage may be raised (with supplementary potassium), if and as necessary, to 250 mg. three or even four times a day. My usual maximum dosage of chlorothiazide for hypertension therefore is 750 mg. to 1 Gm. a day. This is considerably smaller than the doses usually advocated, especially for congestive failure. An additional point is that by dividing the total daily dose into four separate parts apparently a better hypotensive (and diuretic) effect may be achieved with less drug than by giving the total dose all at once. Presumably this is because the kidney rapidly excretes chlorothiazide below the level of its maximal therapeutic effect. In nonedematous patients, there is no reason for not giving a dose at bedtime, since nocturia does not occur on continued therapy (except perhaps initially). Actually, nocturia may be relieved by giving chlorothiazide in the daytime, apparently because, by producing diurnal diuresis, the drug restores the normal pattern of nocturnal antidiuresis.

Conservative doses also help prevent other less frequent but disturbing side-effects of chlorothiazide. These include hyponatremia, hypochloremic alkalosis, weakness and trembling (related in part to hypokalemia), elevation of the serum nitrogen level, sexual impotence, and nausea and epigastric discomfort. In addition, for chronic continuous therapy I see no benefit in using larger doses of this drug when the addition of some other symptomless agent to the regimen may suffice to restore the blood pressure to the desired level. It is well to remember that chlorothiazide has been used continuously for only one year, and as yet we do not know whether true toxic reactions, sensitivity, or other unfavorable side-reactions may occur only after a longer period of use. It seems prudent therefore to reserve this drug for third or fourth place in the usual trial of hypotensive agents.

Ganglionic Blocking Agents

Starting doses of the many available preparations of ganglionic blocking drugs should be low.[1] They should be added cautiously to a combined regimen of drugs such as those already mentioned only if this regimen already is being given in maximal tolerable dosages and without adequate results. Since ganglionic blocking agents cause postural hypotension, their effects should be judged by taking blood pressure with the patient in the upright as well as in the sitting and recumbent positions. Indeed, the chief hazard from using these drugs is that the patient's blood pressure may collapse, particularly while he is standing, and, if he faints, may cause him to injure himself. In addition, if the patient has vascular disease he may suffer from signs and symptoms of cerebral or coronary insufficiency during such an episode, from which he may or may not have long-term residual effects, apparently depending on the severity and duration of the ischemia resulting from the collapse. Fortunately, serious vascular accidents are not common after the use of ganglionic blocking agents. Nevertheless they can occur, and this should be remembered whenever these drugs are being considered for a given patient. Every patient should be warned of the possibility of a collapse reaction, especially on

standing, and should be cautioned to lie down if he feels weak or faint after taking a blocking agent and then to reduce his dosage of the drug.

As with other types of hypotensive drugs, familiarity with one or two preparations as to the dosages and actions in the particular patient under treatment is the most important factor in their successful use. In my hands pentolinium seems to be somewhat more effective in the average case than any other single ganglionic blocking agent. However it may not be tolerated by a given patient as well as some other preparation, or, rarely, it may appear to be quite inactive. In such an instance the use of chlorothiazide should be considered, if it is not already being used, since it may restore the patient's reactivity to the ganglionic blocking agent. If chlorothiazide is not effective and if the urgency to lower blood pressure remains great, another blocking agent may be tried. Pentolinium is initiated in a dose of 20 mg. and is increased by 10 mg. per dose (separated by at least six hours) until some postural hypotensive effect is achieved. At this point further increases in dosage are made very cautiously if and as necessary.

General Precautions

There are some general precautions that should be considered in the management of any patient under antihypertensive treatment.

1. Take time. Persistence is the first requirement for success.

2. Be gradual. Institute drugs and change doses gently. As a rule, sudden changes in blood pressure are not well tolerated by hypertensive patients, particularly elderly ones who may have vascular disease and are subject to vascular accidents.

3. Be satisfied with a reasonably satisfactory objective; do not demand a normal blood pressure in every case. A diastolic pressure of 100 mm. Hg or lower is usually adequate. This also is particularly true in elderly patients who may have had hypertension for years.

4. Be content with a given, reasonably satisfactory regimen. Do not switch over to every new drug that becomes available. Again this warning is particularly pertinent in elderly patients, especially with respect to the use of chlorothiazide and ganglionic blocking agents. If an elderly patient is doing well clinically, let his regimen alone, especially if his disease has not progressed for several years.

5. Use drugs in combination if necessary; do not be too much of a purist. Like it or not, antihypertensive drugs usually work better and with fewer side-effects when used in combination than when given singly. But do not use more drugs than necessary.

6. Hypotensive drugs, except for the ganglionic blocking agents and possibly chlorothiazide, tend to increase gastric secretion and may aggravate if not actually cause peptic ulcers. Antacids should be given to all patients known or suspected to have an ulcer, if they are to be treated with hypotensive drugs. Antacids might well be considered in every patient under such treatment.

7. Weight gain is particularly apt to occur in patients on therapy with Rauwolfia or reserpine. Since weight reduction is to be encouraged in overweight hypertensive patients and weight gain is to be prevented in all, patients should be encouraged to go on a low-fat diet (eliminating fats as far as practicable). This is a relatively easy way of counteracting the weight-gaining effect of Rauwolfia and, for what it is worth, may possibly help offset a tendency to hyperlipemia and atherosclerosis.

8. Reducing the dose of an offending drug is usually preferable to adding a counteracting drug. For example, it is usually better to reduce the dose of reserpine than to add an "energizer" in cases of excessive sedation. Similarly, except for the use of laxatives to decrease constipation, it is better to reduce the dose of a ganglionic blocking agent than try to counteract all its side-effects with a parasympathomimetic agent. In this connection it is well to remember that chlorothiazide may lessen the necessary dosage of a blocking agent and in addition may have hypotensive effects of its own.

9. Other "vasodilating" or "hypotensive" influences such as hot weather, fever (as from infections), alcohol, dehydration (as from diarrhea), starvation, or a strict low-sodium diet may act additively with hypotensive drugs to lower blood pressure unduly. Patients should be warned to reduce their doses of drugs if they catch cold, or have the "flu," with or without diarrhea. The physician may wish to reduce their doses in the spring and summer but may wish to raise them again in the autumn. Alcohol should be used moderately if at all.

10. In time, with or without taking and recording his own blood pressure, an intelligent patient may become quite expert in managing his own antihypertensive regimen. It is well gradually to acquaint him with the actions and side-effects of each agent. However, he should be discouraged from making any sudden or drastic change in his regimen unless he finds himself in serious difficulty. A steady smooth course is desirable, and this can be attained only if the patient leads a smooth life and takes his medicaments steadily. The patient should be encouraged to tell the doctor "all"; in this way he and his physician learn how best to control his blood pressure with the least side-effects. A reasonable compromise, not perfection, is usually obtainable in most cases.

11. Continue to try to reduce dosages of drugs or omit them altogether if and as this can be done without an unfavorable effect. There is no question that "it is easier and requires less medication to keep a blood pressure down than to get it down." Even though later it may be necessary, especially

during stress or in cold weather, to resume a heavier schedule of drugs, reducing the dosage as much as possible undoubtedly is beneficial not only psychologically and physically but financially as well. The watchword in drug therapy is always to use the minimum that is effective.

Summary and Conclusions

Proceeding from the milder to the stronger antihypertensive drugs, one may try successively and in combination Rauwolfia, Veratrum, hydralazine, chlorothiazide, and a ganglionic blocking agent. By using minimal effective doses in combination, a safe and asymptomatic regimen can usually be found that will achieve a reasonable lowering of blood pressure. Dosages and changes in dosages should be instituted gradually. Repeated attempts should be made to reduce dosages or omit drugs altogether when this can be done without a rise in blood pressure. Caution should always be exercised, particularly with the stronger agents and with continued long-term therapy. How they are used is the most important single factor in the successful use of these agents. Each drug may be employed in combination with other therapy.

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RENAL RESPONSE TO EXERCISE—URINARY FINDINGS

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The albuminuria that frequently occurs in athletes after severe exercise has been observed not only in contact sports but also in sports like rowing, which are nontraumatic and certainly involve no body contact. This study concerns urinary findings after severe exertion at rowing, swimming, lacrosse, track, and football. The percentage of athletes having albumin, red blood cells, and casts in their urine after severe exercise was similar in all five sports. With respect to the finding of red blood cells, swimming, lacrosse, and track were about the same (80%), and football and rowing about even (55%). The 1,500-meter swimmers and the long distance track men showed the greatest amount of all three abnormal urinary findings. The duration of the event played a major part in determining the degree of the abnormality, and in the 1,500-meter race especially the urine was often loaded with red blood cells and casts. These usually disappeared within 24 hours, but the question is raised whether kidneys handicapped by previous infections can go through such experiences without cumulative damage.

Fifty years ago albuminuria, characterized as functional, was reported to occur in athletes after severe exercise.[1] A later study[2] found albumin, casts, and red blood cells in the urine of marathon runners and baseball players. Recently studies of football players[3] and boxers[4] have shown similar findings. These were all sports which carried with them some direct trauma to the kidneys such as jostling or shaking of the kidneys in marathon runners and direct blows in football and boxing contests. The football and boxing reports emphasized the red blood cells as a result of trauma. The report of Boone and associates[5] on hematuria in football players suggested to one of us (E. P. A.) that perhaps the red blood cells were not after all due to trauma as supposed, but to the response of the kidneys to the severe exercise itself. For that reason a rowing crew was studied and the findings reported.[6] Rowing is a sport which is truly nontraumatic to the kidneys, so that these findings were interpreted as being the result of the severe exercise alone.

Gardner,[7] reporting on athletic pseudonephritis, suggested that the urinary findings in football players are exactly the same as those in acute glomerulonephritis. The only way of distinguishing the two is the disappearance of these abnormal

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findings within a week after football scrimmage has been discontinued. It may then be assumed that this was not a nephritis. His figures on football players compare closely with those of Boone. Thus, in exercises where there is considerable body contact, such as football, boxing, horseback riding, or jeep riding over rough territory, there is actual trauma to the kidneys superimposed on the physiological changes due to the exercise alone. This type of exercise naturally may increase the amount of blood in the urine of injured players. But is the percentage of players with blood higher than in noncontact sports? Stimulated by the results of the experiments with the crew men, we have just completed a study of swimmers. This sport we also consider as being nontraumatic to the kidneys. Track

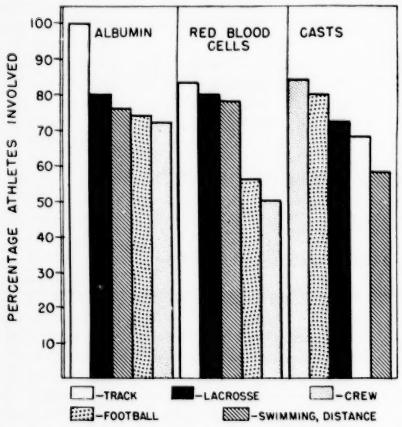

Fig. 1.—Relative percentages of athletes showing urinary sediment after engaging in sports.

and lacrosse were also investigated. The former may be questionable as to direct trauma, but certainly the latter is traumatic.

In all of these sports the contests are intercollegiate matches in which the maximum amount of effort is put forth. Figure 1 is a summarized composite graph of the five sports. The striking thing is the similarity in urinary findings in all these sports. Between 60% and 80% of these athletes have albumin, red blood cells, and casts in their urine after severe exercise. It is also evident that there is not much difference in the percentage of athletes with red blood cells in their urine, whether the sport is renal traumatic or nontraumatic in character. Swimming, lacrosse, and track are about the same (80%) and football and crew about even (55%). However, participants in football and boxing often had red blood cells greater in numbers than those in the other sports, for some of them had gross hematuria. This we assume was due to direct renal trauma.

All of these specimens were examined by us personally and with considerable time and care. Perhaps this accounts for the finding of such a high percentage of red blood cells and casts in the urine. If careful search is made, it is not rare to find a faint trace of albumin and/or 1 to 2 red blood cells per high-power field in the urine of normal individuals. Hence these slight variations were not considered particularly abnormal. Gradations on the charts are made in the following manner: 1. Albumin: 0 to trace, considered none. Recordings were made according to 1+, 2+, 3+, and 4+ levels. 2. Red blood cells: 0 to 2 per high-power field in the centrifuge specimen was considered negative. Recordings of 3 to 5 per high-power field and then all over 6 per high-power field were made. 3. Casts: 0 to 2 per high-power field, considered negative; 3 to 5 per high-power field, and those over 6 per high-power field are charted. These urine specimens were collected immediately after the contest by us personally. The albumin and microscopic examinations on the centrifuged specimens were carried out by us at once.

Results

Figure 1 shows the relative percentages of the number of athletes engaging in lacrosse, football, rowing, track, and swimming. The striking over-all picture of this chart is that, in all sports, between 50% and 80% of the contestants showed albumin, casts, and red blood cells in the urine. Albumin was present in about equal percentages, between 70% and 80% of all sports, with the exception of long-distance track with 100% albuminuria. As to the red blood cells in the urine, the long-distance track, lacrosse, and swimming are grouped together at about 80%; football and crew had about 50%. One is perhaps surprised that not a higher percentage of football players had red blood cells in their urine, since it is a rough contact sport. But the variable factor which is significant in football is how long did the man play in the game and how much exertion did he really put forth. For instance, a player might get in a game for just a few minutes and not exert himself very much at that. He would probably not have the abnormal findings in the urine that a long-distance track man would who ran hard for two miles. The amount of energy put forth by these two individuals would be entirely different.

On the other hand the amount of actual blood in the urine, in many of the football players, was more than in the other sports. This was probably due to the addition of a contact trauma to the kidney itself. This would be true also in lacrosse. The fact that our lacrosse players have a higher percentage of red blood cells than football men similarly de-

pends on the fact that the players in lacrosse were constantly active while in the game and there were few substitutions. These athletes played most of the game and had a much longer duration of active exercise than the football players. All the sports showed between 60% and 85% of the participants having casts in the urine. Generally, we can say that the urine which contained much albumin usually was loaded with casts and red blood cells. In a few instances, this was not necessarily so. Two or three had a lot of albumin, many casts, and only a few red blood cells. However, this finding was not the rule.

In figures 2, 3, and 4, each small column represents one athlete. At a glance one can tell how many men had that amount of albumin, red blood cells, or casts in the urine. Figure 2 shows the urinary findings in swimmers in intercollegiate contests. They are divided into the short events of 50 to 100 yards and the distance events of 440 yards and 1,500 meters. It is quite evident from a glance at these charts that the length or duration of the event plays a major part in the degree of the abnormal findings. For instance, in the 50-to-100-yard short swimming events, all of the swimmers had some albumin but it was only a little, and a good percentage of them had very few red blood cells and casts. In the distance events, the 440-yard and particularly the 1,500-meter race which calls for a tremendous amount of energy output, the number of athletes whose urine contains a 3+ albumin and is loaded with red blood cells and casts is very much higher.

The 1,500-meter swimmers and the long distance track men showed the greatest amount of all three abnormal findings in the urine. Of the nine long-distance swimmers examined, six of them had 3+ albumin, three of them had 6 to 10 red blood cells, and four were loaded with red blood cells: two of these were loaded with casts and three had 3 to 5 per high-power field. These were the outstandingly high quantitative abnormal findings in the urine of all the athletes. In contrast to this are the findings in 11 short-distance contestants. In the short-distance swimmers there were 3 out of 11 who had from 6 red blood cells to loaded as compared with 7 out of 9 for the distance swimmers. Swimming is considered a noncontact sport, so the higher percentage and amount of red blood cells in the distance swimmers is of real significance. It must be the result of the renal response to the exercise alone, and not from any contact renal trauma.

Track.—Track is considered a partially noncontact sport because without doubt the kidneys receive some trauma from the continual jogging up and down during a long-distance race. Figure 3 is divided into short-distance and long-distance events. Individual columns show the 100, 220, 440, and 880 yard and the 1-mile and 2-mile races. One can study this chart in the vertical manner and so compare the differences of the amount of albumin, red blood cells, and casts in short and distance events. By horizontal study one can see either the albumin, the red blood cells, or the casts separately in the various distances, from the 100-yard sprint to the 2-mile race. Scanning the chart in the vertical manner, it is apparent that in the 100-yard dash there are practically no abnormal findings. True there were three who showed some red blood cells and three showed some casts, but they were from 0 to 2 per high-power field. The

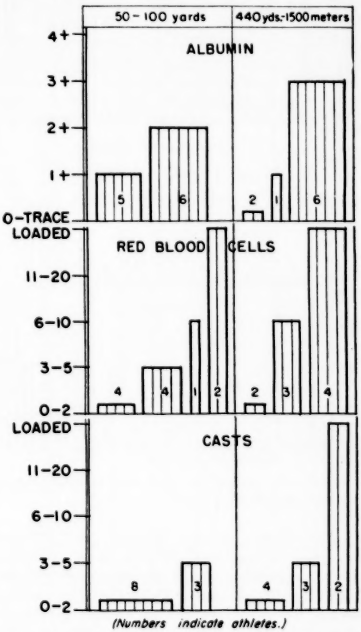

Fig. 2—Urinary findings in swimmers in intercollegiate contests, short and distance events.

albumin was only a trace. As one progresses with the distance of the races, from the 220-yard to the 2-mile, in the vertical manner one sees an increase in each after the 220-yard. Beginning with the 440-yard race, all three findings are markedly increased. In the mile race, it is evident that both the number of athletes involved and the degree of abnormalities are precipitously higher. For instance five out of six of the milers had a 3+ albumin. Three out of the six had 3 to 5 red blood cells, and one had 11 to 20 per high-power field. The casts similarly increased: four out of six had from 3 to 10 per high-power field. In the 2-mile race one had a 2+ and

one had a 4+ albumin level. Both of them had red blood cells 6 to 10 per high-power field; one had 6 to 10 casts per high-power field, and the other was loaded with casts.

Scanning this chart horizontally, one can compare the amount of albumin in all of the various races starting from the 100-yard dash and progressing to the 2-mile. In the 100-yard and 220-yard dashes, there is very little present. In the 440-yard, it rises considerably. This is also apparent with the red blood cells and casts. These findings are also evident in the 1-mile and 2-mile events. It is apparent that the longer and more strenuous the race, the greater the percentage and degree of abnormal urinary findings.

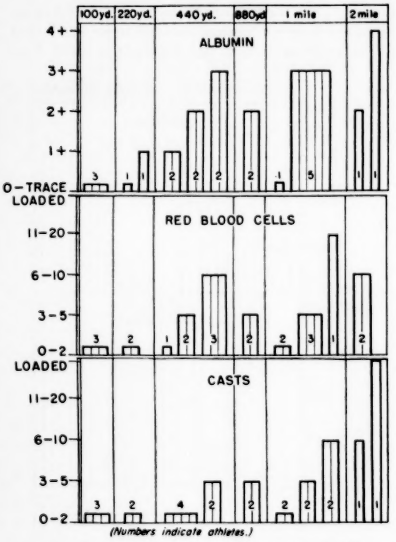

Fig. 3—Urinary findings in track men in intercollegiate contests, short and distance events.

Lacrosse.—Lacrosse is definitely a contact sport. It is a strenuous game with few substitutions or chances for rest. Out of the 16 players there were only 3 who had 0 to trace of albumin, 6 had 1+, 2 had 2+, and 5 had 3+ levels. In the red blood cell counts, four had from 0 to 2, four from 3 to 5, six from 6 to 10, and two over 11 per high-power field. The casts were quite prominent in this sport. Five men had from 3 to 5 per high-power field, one had 11 to 20, and six players were loaded with casts. Here, too, it was noted that the men who played the hardest and the longest were the ones who had the most albumin and casts in the urine. It is also interesting to note that one game was played on a cool, pleasant, breezy day and another on a very hot, humid afternoon. The abnormal urinary findings were definitely higher on the hot day. This was also evident in our studies on the crew men.

Rowing.—Rowing was the first true noncontact sport which one of us (E. P. A.) studied and reported.[6] This study was carried out on four college crews after two practice races and after one intercollegiate race. In the practice session, 31 men were examined before and after exercising, and 16 before and after the intercollegiate race. All the urine specimens before the races were normal in all respects. The relative percentage of the three races are summarized in figure 1. Of the 40 men showing albumin after the intrasquad races, 27 had only a trace and 13 had a 1+ level, 17 or 55% of the men had 1 to 4 red blood cells per high-power field, and casts were found in 16 of these 17 men. After the intercollegiate race, 13 of the 16 men showed albumin, and of these 13, 4 had a trace and 9 had a 1+ to 2+ level. This would seem to show that after an intercollegiate race, which brings forth more effort and severe physical exercise than the intrasquad practice races, the percentages were higher and the degree of abnormalities greater. This difference was also noted in the amount of red blood cells and casts.

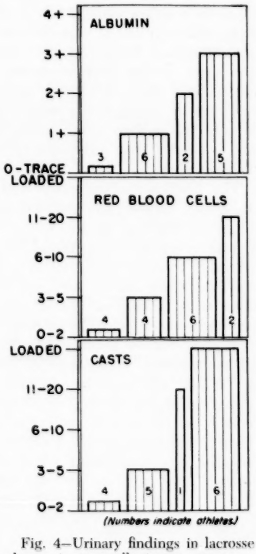

Fig. 4—Urinary findings in lacrosse players in intercollegiate contests.

Comment

The striking thing in these investigations is the apparent uniformity of the findings of albumin, red blood cells, and casts in the urine of most athletes after strenuous exercise. In the traumatic sports such as football, lacrosse, and boxing, trauma may increase the actual number of red blood cells in the urine to a gross hematuria, but the actual percentage of athletes with microscopic hematuria is no higher in those sports than in the

nontraumatic sports. Another interesting fact is the uniformity of these abnormal urinary findings contrasted in exercise of short and long durations. This is true in both track and swimming. The difference in findings in the 100-yard and 220-yard dashes as contrasted with the 440-yard, 880-yard, 1-mile, and 2-mile events is evident. The men in the 50-yard and the 100-yard swimming events showed more abnormal findings than the 100-yard track men, evidently because there is much more energy put forth by the swimmers. However, the short-distance swimmers showed less albumin and fewer casts than the long-distance swimmers, such as in the 1,500-meter events. Some of these mile swimmers had a very heavy albuminuria and the microscopic fields were loaded with casts and many red blood cells. The amount of albumin and the casts were the most striking findings. This is also found in the lacrosse players.

It is interesting to speculate from this study whether the slightest injury to the filtration mechanism permits the albumin to leak through and as the injury progresses because of increased exercise the red blood cells and the casts then appear. This seems apparent in the short-distance swimmers. Many of them had few or no red blood cells and casts, but all 11 had albumin, 5 had 1+, and 6 had a 2+ level. This is also suggestive in the track chart. It is believed, and has been proved in track men and in our football and crew studies, that the urine returns to normal within 24 to 48 hours after discontinuing the exercise. However, this particular point was not investigated in this present study.

We thought it would be interesting to determine whether any of this renal response to exercise was related to the nervous state of the individual engaged in these intercollegiate contests. Therefore, we took as test subjects four female college freshmen who were taking their first examination in college. After talking with them, we were convinced that they were just about as highly nervous and tense as anyone could be. Specimens were obtained immediately after their examinations and examined in the usual manner. None of these girls' specimens showed any albumin, casts, or red blood cells. We feel, therefore, that the response obtained in our subjects during exercise is not effected by the slight outpouring of epinephrine which might occur during the period of nervous tension and excitability, but rather is dependent upon the physical exercise itself.

The cause for the presence of albumin, red blood cells, and casts in the urine after severe exercise is not definitely known. There have been interesting hypotheses substantiated by considerable experimental research. It is known that during exercise the blood leaves the splanchnic area and various organs including the kidneys. It is shunted into the main circulation, to the heart, to the lungs and to the muscles involved in the exercise which demand it for their increased metabolism. It is well known that there is a marked decline in the renal plasma flow and the glomerular filtration rate. In severe exercise the plasma flow may be reduced as much as 50 to 75%. Boyarsky [7] reported that in studies on traumatic shock carried on during World War II, half of the patients with a mean blood pressure of 50 mm. Hg showed a reduction in renal blood flow of 30% to 80%, and the remainder showed a more profound reduction. Furthermore, hypoxic damage to the nephron may result from the marked lowering of the renal blood flow. In the dog a 90% reduction in renal blood flow is a critical level below which acute renal failure can be expected to appear, if the reduction persists. Therefore, it is evident that the degree of vascular diversion from the kidney during severe exercise approaches that seen in traumatic shock.

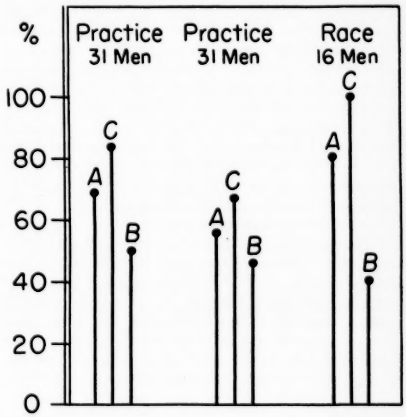

Fig. 5.—Urinary findings in crew men after two practice exercises and an intercollegiate race. A=albumin; B=red blood cells; C=casts. Reproduced with permission of *Southern Medical Journal* (**50**:905-909 [July] 1957).

Chapman and co-workers [8] showed that this reduction does not remain for long. Within an hour after the exercise is stopped, there is a return of the plasma flow to within 10% of the preexercise level. Barclay and associates [9] report a drop in the glomerular filtration rate of 44.6% after exercise. They postulate that the primary change is the constriction of the afferent arterioles. After this there is a compensatory constriction of the efferent arterioles in order to maintain a filtration rate in the face of a falling renal blood flow. In this way the glomerulotubular balance is not upset. The renal vascular channels definitely constrict, and this causes the considerable decrease in the renal blood flow. It may drop from a normal of 1,000 cc. per minute at

rest to 200 cc. per minute during exercise. Hence 800 cc. or more of blood per minute is shunted to the active organs where it is most needed.

The constriction during light and moderate exercise is probably a response to specific nerve impulses only. The marked constriction caused by the addition of epinephrine occurs only when the exercise becomes severe. Intravenous administration of arterenol and epinephrine were given to several subjects and measurements made of the renal plasma flow, glomerular filtration rate, urine volume rate, and protein excretion. In their study, King and Baldwin [10] showed the following findings: 1. Transient proteinuria of short duration occurred in all subjects from both arterenol and epinephrine. 2. The injection of epinephrine and arterenol also produced a reduction in renal plasma flow, glomerular filtration rate, and urine volume, with an increase in filtration fraction. 3. The over-all increase in renal vascular resistance occurred in all of these patients, predominately afferent in the case of arterenol and equally afferent and venular with epinephrine. 4. The maximum tubular reabsorptive capacity for glucose is unaffected by arterenol. This is taken to indicate that the renal ischemia is diffuse and involves all of the nephrons and is not selective in character. It would be interesting to determine the pyrocatechin level in the urine of the athletes to see if arterenol plays some part in the vasoconstriction during exercise.

White and Rolf [11] found similar results in PAH and inulin clearance tests after exercise. They both fell markedly, and the renal vascular resistance increased at least fivefold. In these experiments values returned to normal within one hour after the cessation of the exercise. The albumin did not appear in the urine until after the exercise was completed. This suggested the theory of a differential constriction of the renal vascular channels. During exercise, some of the glomeruli may have no blood flow or a capillary pressure too low to permit filtration. Then when the flow and filtration are reestablished after the exercise is over, the albumin appears in the filtrate of these so-called damaged glomeruli. If the blood flow is uniformly reduced by vasoconstriction through the glomerulus, one would expect the albumin to appear during the period of greatest ischemia. This could be proved if it could be shown that the glucose tubular maximum capacity is reduced during exercise. For in health, the constancy of glucose tubular maximum for the reabsorption of glucose suggests that all the nephrons are functioning. If this drops, some of the glomeruli must be nonfunctioning. This would be in favor of the selective constriction theory. King and Baldwin [10] showed that in their subjects the maximum tubular reabsorptive capacity for glucose is unaffected by arterenol, indicating that the renal ischemia diffusely involves all of the nephrons.

Proteinuria is evidence of damage to the glomerular filtration mechanism which has not been compensated by the tubular reabsorption as is normally carried out. The nature of the protein excreted during exercise may shed light on the size of the glomerular pore allowing its passage, whether it is a normal membrane or an anoxic rupture. This can be determined by the method of paper electrophoresis. Boyarsky [7] hypothesized that during severe renal ischemia, the tubules become unsaturated in respect to the load received from the glomerulus, since the filtration rate has fallen to low levels. The tubular reabsorption becomes excessive. The urine flow diminishes greatly and the urine becomes overly concentrated. In patients in shock, even though the renal blood flow drops to 5%, urine formation still continues. This does not cease until the renal blood flow stops. Therefore, he concludes that the cylindruria is evidence of inspissation of protein in the tubule due to the diminished urinary volume or complete stagnation. The morphologic picture of the kidney after ischemic injury is a focal necrotic lesion located at any portion of any tubule as if by chance. It has been called "tubulorrhexis." It shows the disruption of the basement membrane and the tubular cells so that there is a gaping hole which could serve for back flow of urine or as a tubular venous anastomosis.

It is doubtful that this is what takes place after exercise because of the rapid recovery of the tubular cells. Usually within 24 hours the albumin, casts, and red blood cells have disappeared from the urine. This could be studied by the renal biopsy method in experimental animals. The finding of albumin in the urine in conditions other than definite renal disease is not uncommon. For instance, orthostatic albuminuria in the tall, asthenic young man is probably due to circulatory changes resulting in diminished renal blood flow. Such transitory albuminuria is inconsistent with the idea of tubulorrhexis. Would an actual rupture of membrane or cells heal so promptly? However, the large amounts of red blood cells, albumin, and casts in the urines of the distance swimmers and track men after severe prolonged exercise make us believe that under such circumstances there is definite renal damage. Boyarsky states that whether this is evidence of minute foci of renal destruction, which is not noticed because of the normally large renal reserve, or is a damage on the cellular level, which is readily reversible, we can not say.

In addition to the above-mentioned changes in the urine, after exercise, Hyman and co-workers [12] reported an increased exfoliation of epithelial cells. Many of these cells come from the deeper layers of the bladder epithelium. The cause suggested is that the urine swirling over the bladder mucosa mechanically causes an increase in this exfoliation. Certainly there can be no effect on the tissues

themselves. It is a purely local condition in the bladder and not due to lesions elsewhere in the urinary tract.

Conclusions

The above results in the sports of rowing, football, track, lacrosse, and swimming show the constancy of the abnormal elements in the urinary sediment. Disregarding the theoretical cause, the fact remains that, at least temporarily, there is damage to the kidney. Whether this leaves the tubular element in a weakened or more vulnerable condition cannot be proved. We are inclined to believe that it does. The recovery seems to be prompt, but is it complete? The question arises as to whether anyone who has had definite renal disease such as acute glomerulonephritis or pyelonephritis should indulge in severe physical exercise. Exercise at least temporarily adds additional damage to the already injured renal cellular elements. We can recall two such instances of men who continued to indulge in severe physical exercises in intercollegiate athletic contests after having had acute nephritis. One of these men died in renal failure within 5 years and the other within 15 years of the acute renal disease. Both of these men had apparently recovered from their acute nephritis. They returned to college and again took active part in intercollegiate athletics. The question is, was the renal failure hastened by the added strain of exercise? Another patient had an attack of acute pyelonephritis. This apparently cleared up promptly on chemotherapy, as shown by negative cultures and negative microscopic stained smears. Within two weeks she began playing strenuous tennis singles. She had a relapse the day after such a contest. Is it advisable for anyone who has had acute renal injury to ever indulge in severe physical exercises? Is it not adding insult to injury? We believe that we should recommend limitation of exercise in patients with impaired renal function or history of acute or chronic parenchymal renal disease.

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AIR POLLUTION AND PULMONARY CANCER.—Carcinogenic agents belonging to the group of polycyclic aromatic hydrocarbons, to the aliphatic epoxides, and to inorganic compounds containing chromium and nickel have been identified in the atmosphere. One of the most ubiquitous of the carcinogenic agents belonging to the polycyclic aromatic hydrocarbon group of chemicals is 3,4-benzpyrene. It is derived as an atmospheric pollutant from many sources including gasoline and diesel engine exhausts, soot secondary to the incomplete combustion of organic matter, soot incidental to rubber-tire wear and tear and degradation, and in isolated areas as specific industrial effluents in the manufacture of coal tar and its derivatives. The aliphatic materials are primarily introduced into the atmosphere as a result of pollution by raw gasoline vapors. These vapors, under certain meteorologic conditions, react in the presence of sunlight and oxides of nitrogen to form a broad spectrum of hydrocarbon oxidation products. Chromium and nickel though present in infinitesimal amounts nevertheless must be considered by virtue of occupational and experimental data incriminating them as carcinogenic agents. It must be remembered that one of the critical factors in eliciting the carcinogenic responses is the concentration at which these agents are present.—H. L. Falk, Ph.D., Pulmonary Cancer with Special Reference to Air Pollution and Pathogenesis, *CA Bulletin of Cancer Progress*, March-April, 1958.

DIURETIC ACTION OF TWO CARBONIC ANHYDRASE INHIBITORS IN CONGESTIVE FAILURE

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Two carbonic anhydrase inhibitors, acetazolamide and ethoxzolamide, were compared with intramuscularly given meralluride by oral administration in a group of ambulatory patients with congestive heart failure, with the criterion of response being the loss of body weight during the first 24 hours after the dose. The maximum diuretic response to acetazolamide was equal approximately to that given by 0.5 cc. of meralluride; the response to ethoxzolamide was somewhat greater, equal approximately to that given by 0.7 cc. of meralluride. The diuretic responses to the two carbonic anhydrase inhibitors were similar when they were given in doses which caused approximately the same incidence of unpleasant symptoms. The maximum diuretic effect of acetazolamide was obtained from a dose of 125 mg. No greater effect was obtained from a dose eight times larger. It was found that orally given acetazolamide neither increases nor diminishes the diuretic response to intramuscularly given meralluride.

Since the report by Friedberg, Taymor, Minor, and Halpern [1] on the use of acetazolamide (Diamox), a specific carbonic anhydrase inhibitor, as an orally given diuretic in patients with congestive heart failure, the investigation of this class of compound has rapidly advanced and many publications have appeared describing their pharmacology and clinical applications. Several new members of the carbonic anhydrase inhibitor group have been tested, although most of the reports relate to acetazolamide. While agreement is general that this compound produces diuretic effects which prove useful in milder cases of congestive failure although insufficient in more advanced cases, there remain unsettled problems which are in need of more study before the final place of these materials in diuretic therapy is established. More needs to be known about their potency in relation to a standard and to other orally given diuretic agents, the most favorable dosage and dosage plans, and their effect when used together with other diuretic agents. In previous reports,[2] we described a method of bioassay of diuretic agents in ambulatory patients with congestive failure. We have now applied this method in an examination of acetazolamide and of a new chemically allied carbonic anhydrase inhibitor, ethoxzolamide (Cardrase). The results form the subject of this report.

Method of Bioassay

We adapted the conventional principles of pharmacological assay on animals to the assay of diuretic agents in patients with congestive failure. The test drug is compared with a standard—intramuscularly given meralluride (Mercuhydrin) sodium—in a group of 25 or more ambulatory patients with congestive failure in attendance at our cardiac clinic. The criterion of response is the body-weight loss in the first 24 hours after the dose. This closely parallels the curve of clinical improvement in patients with congestive failure.[3] The patients are accurately weighed, receive a dose of the drug, either meralluride given intramuscularly or the particular test-drug, and are weighed again 24 hours later. They return for a dose of the drug at weekly intervals. These patients are instructed to remain on their usual diet, with free water intake and salt restriction. Most of them also receive a daily dose of a digitalis glycoside. This regimen remains unchanged during the assay. In each group of patients, several dose-levels of the standard and of the test-drug are administered in randomized fashion. The average weight loss for the group with the various doses provides data for dosage-response curves for both the standard and the test-drug in the same patients. The potency of the test-drug is expressed in terms of the standard. Differences in response are tested for significance by standard statistical methods. In the case of the assay of orally given diuretics which may produce disagreeable symptoms from their local actions, an inert placebo tablet indistinguishable from the test-drug is included in the assay by the double-blind technique.[4]

Acetazolamide—Potency and Dose

In the clinical evaluation of this material, Friedberg and others [1] used single doses as high as 0.75 Gm. three times daily for two or three days and as low as 0.25 Gm. daily continuously for longer periods. They found the 0.25-Gm. dose as effective as the higher ones. They observed in their group of 26 patients that about 70% showed a diuresis, weight loss, and clinical improvement, which compared favorably with the results of a mercurial diuretic given parenterally. Belsky [5] found acetazolamide a satisfactory substitute for

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the 2-cc. injection of meralluride in 11 of 13 patients with congestive failure treated for prolonged periods. He used a daily dose of 1 Gm., which caused some toxic effects, but in two cases he also observed that the 0.25-Gm. daily dose was equally effective and suggested that this dose might prove the most favorable for both starting and maintaining the treatment. The fact that in these studies there were patients in whom acetazolamide proved unsatisfactory so that the return to the mercurial injection was necessary points to the limited diuretic action of acetazolamide as compared with the organic mercurial. Clinical experiences such as these are useful but do not provide a quantitative value for the relative diuretic activity of different materials. Moyer, Ford, and Spurr [6] compared orally given acetazolamide with meralluride injection in terms of the 24-hour increase in sodium excretion in patients on a fixed salt and water intake. Their chart shows that the 0.25-Gm. dose of acetazolamide produced only about one-fourth the effect of an injection of 2 cc. of meralluride. They observed that larger doses produced no greater effect. They further observed [7] that the 0.25-Gm. orally given dose of acetazolamide produced the same effect as a dose of 3 tablets (30 mg. of nonionic mercury) of an orally administered mercurial diuretic, chlormerodrin (Neohydrin). This also indicates a restricted order of potency of acetazolamide since, in our bioassay,[2b] more than twice as much chlormerodrin given orally produced diuretic effects equal to 0.71 cc. of intramuscularly given meralluride. In contrast with these findings is the report by Cardillo, Mullin, Schiffer, and Lyons.[8] They carried out a bioassay in accordance with conventional principles and compared orally given acetazolamide with an injection of mercaptomerin (Thiomerin) sodium in terms of the 48-hour weight loss in 25 ambulatory patients with congestive failure. With respect to acetazolamide their results show that the 0.5-Gm. dose caused nearly twice the effect of the 0.25-Gm. dose (ceiling effect at about 0.5 Gm.). Their results further indicate that acetazolamide is more effective than the injection of mercaptomerin, the 0.5-Gm. dose caus-

Incidence of Toxic Symptoms After Oral Administration of Two Carbonic Anhydrase Inhibitors

	Dose, mg.	Doses Given, No.	Patients Reporting Symptoms, % None	Minor	Major
Acetazolamide	125	154	88	11	1
	250	188	85	12	3
	500	38	71	10	19
	1,000	37	65	14	21
Ethoxzolamide	62.5	42	98	2	0
	125	89	71	19	10
	250	47	51	26	23

ing more than twice the effect of the 1-cc. injection of mercaptomerin, the maximum effect greater than the 2 cc. of mercaptomerin (approximately the ceiling dose of the organic mercurial injection [9]). This result with mercaptomerin could be an artifact due to the method, the use of the weight loss over a 48-hour period, the acetazolamide having been given for two days and the mercaptomerin for only one day per week. Since a large part of the weight loss from a dose of mercaptomerin is recovered on the second day, their results

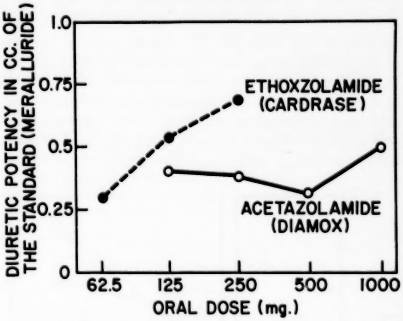

Fig. 1.—Diuretic potency of two carbonic anhydrase inhibitors in terms of intramuscularly given meralluride in patients with congestive failure; 24-hour weight loss is index of effect. Position of points on curves was obtained by comparing average weight loss for group at each dose level with dosage-response curve of intramuscularly given meralluride administered concurrently to same patients.

may have involved a comparison of the maximum effect of acetazolamide with only a partial effect of the organic mercurial.

Dosage-response curves are an essential part of a satisfactory bioassay. Ford, Spurr, and Moyer [7] stated that the range of doses of the anhydrase inhibitors for the minimal (threshold dose) and maximal ("apex point" or ceiling dose) action of increasing salt and water is so small that it is impossible to establish a satisfactory dosage-response curve. Cardillo and others [8] obtained a favorable dosage-response curve with acetazolamide, with use of the criterion of the 48-hour weight loss. We failed to obtain a dosage-response curve with the 24-hour body weight loss as an index and did not pursue the experiment to a definitive bioassay, although it is probable that a dosage-response curve would have been obtained if smaller doses had been tried. As far as we have gone, however, the results give a fairly good indication of the diuretic potency of acetazolamide in terms of the effect of injected meralluride. Our ambulant group of patients with congestive failure received a total of 417 doses of acetazolamide, ranging from 125 to 1,000 mg. each (see the table and fig. 1). The diuretic response was indistinguishable over the eightfold range of doses, all producing a diuresis equivalent to less than that with 0.5 cc. of intramuscularly given meralluride. The dose of acetazolamide for the maximum average diuretic response (ceiling dose) is here on the order of 125 mg. or less. This corresponds to the findings of

Ford, Spurr, and Moyer [7] and is at variance with the observations of Cardillo, Mullin, Schiffer, and Lyons.[8]

Combined Action of Meralluride and Acetazolamide

There are many reports in the literature on the combined administration of various diuretic agents in the endeavor to increase the therapeutic effect. In previous studies we applied our bioassay method in a comparison of meralluride alone with meralluride and ammonium chloride [10] and meralluride and aminophylline.[11] Both of these drugs, as others have observed,[12] were found to enhance the diuretic effect of the particular injection of meralluride. We have now tested acetazolamide in the same way. The results are shown in figure 2. The acetazolamide was given in doses producing average maximum diuretic effects, 125 and 250 mg. each. The effect of the acetazolamide alone was compared with that of an inert placebo tablet. The points relating to this in figure 2 are based on nine randomized doses in each of 39 patients. The acetazolamide gave an average weight loss of nearly 1 lb. (0.5 kg.) in 24 hours, which proved to be an unequivocal diuretic effect. The difference between the acetazolamide and the placebo was highly significant ($p<0.01$) by paired t-value analysis. When the tablet of acetazolamide was given together with an injection of meralluride, the diuretic effect proved to be that of the meralluride alone. The three curves in figure 2, one for the meralluride alone and two for the combination with acetazolamide, are substantially similar. This was confirmed by statistical analysis. There were three separate meralluride dosage-response curves, and calculation revealed no significant effect of the acetazolamide on either slope or displacement. By analysis of variance restricted to the four doses that included both drugs, it was possible to show a significant effect for the meralluride but not for the acetazolamide and neither enhancement nor depression of the meralluride effect by acetazolamide. Maren [13] tested the combined action of the two drugs in dogs in terms of sodium excretion and concluded that their primary renal effects are not additive but that metabolic acidosis due to acetazolamide increases the response to meralluride. In a study of patients with congestive failure refractory to meralluride, Rubin, Thompson, Braveman, and Luckey [14] found acetazolamide alone ineffective. The mild metabolic acidosis produced by acetazolamide also failed to restore the diuretic response to meralluride significantly until more pronounced acidosis was produced with the aid of large doses of ammonium chloride.

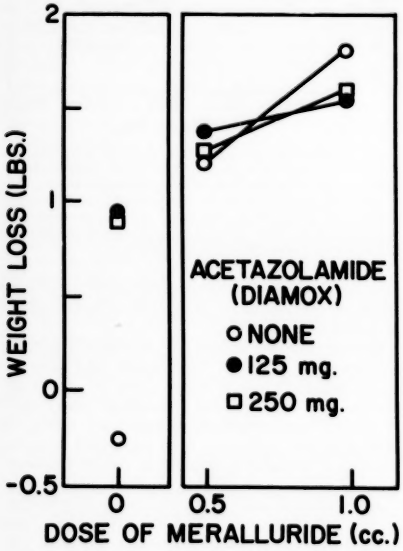

Fig. 2.—Effect of combined administration of meralluride intramuscularly and acetazolamide orally in 39 patients with congestive failure. Acetazolamide does not enhance diuretic response to meralluride.

Ethoxzolamide

Ethoxzolamide, 6-ethoxy-2-benzothiazolesulfonamide (Cardrase), is a new carbonic anhydrase inhibitor which is under consideration for therapeutic use. Chemically, it is closely allied to acetazolamide. Ford, Spurr, and Moyer [7] compared it with acetazolamide in patients with congestive failure, using as an index the 24-hour urinary sodium excretion. With this compound they obtained a conventional dosage-response curve, with increasing effects with doses of 33.75 to 125 mg. and with larger doses up to 500 mg. producing no greater effects than the dose of 125 mg., and they stated that this was substantially similar for acetazolamide. They concluded that the diuretic activity of ethoxzolamide is not significantly different from that of acetazolamide in terms of electrolyte and water excretion and change in body weight.

Our assay was carried out on 42 ambulant patients with congestive failure, the comparison being made with intramuscularly given meralluride in the same patients in terms of 24-hour body-weight loss. There were 178 doses of 62.5 to 250 mg. each. Higher doses could not be tested because of the mounting incidence of disagreeable symptoms. The results are charted in figure 1. A conventional dosage-response curve was obtained. In this assay, ethoxzolamide proved to be substantially more potent than acetazolamide when compared with intramuscularly given meralluride not only from the standpoint of the dose necessary for a particular effect but from the standpoint of the maximal obtainable effect (ceiling response). The 250-mg. dose produced a diuretic response equivalent to that

with approximately 0.7 cc. of intramuscularly given meralluride. There are no facts available at present to explain the higher ceiling response to ethoxzolamide than to acetazolamide, since both are carbonic anhydrase inhibitors. There remains the possibility that an action in addition to anhydrase inhibition may be involved.

Toxicity

The reports in the literature indicate a low order of toxicity for the carbonic anhydrase inhibitors as orally administered diuretics. This is confirmed in the present study. On each clinic visit, every patient received both an intramuscular injection and an oral capsule, at least one being an inert material. All judgments were made against that placebo background 24 hours after the dose by an examiner who did not know the identity of any particular dose (double-blind test). Persistent placebo reactors thus could be discounted, although an occasional report may still include a symptom not caused by the pharmacological action of the drug. Symptoms were classified as "minor" when they did not jeopardize the regimen of treatment (weakness, chills, grogginess, dizziness, dry mouth, flushed face, itching face, tingling fingers, headache, and slight nausea). They were classified as "major" when they were judged severe or disturbing enough to cause some patients to refuse further medication or to continue only under protest (severe nausea, diarrhea, abdominal cramps, and vomiting). The results are presented in the table. The incidence of disagreeable symptoms increased with the dose. It rose with the larger doses of both drugs to approximately one-fifth of the group of patients. A more extensive experience is necessary to establish the relative incidence of toxic effects of the two agents in relation to the doses that produce the maximum diuretic effects.

Summary and Conclusions

The diuretic potency of two carbonic anhydrase inhibitors, acetazolamide (Diamox) and a new compound, ethoxzolamide (Cardrase), in ambulant cardiac patients with congestive failure was determined by comparison with a standard, intramuscularly given meralluride (Mercuhydrin).

The method of bioassay involves a dosage-response curve for the test-drug and the standard in the same group of 25 or more patients in terms of the 24-hour weight loss. This index of effect corresponds to clinical improvement. The validity of differences in response is tested by conventional statistical methods.

The average maximum diuretic response with orally given acetazolamide is obtained from a dose of approximately 125 mg. The average maximum diuretic effect of this drug (ceiling effect) is equivalent to somewhat less than that with 0.5 cc. of intramuscularly administered meralluride. An average maximally effective oral dose of acetazolamide given together with an intramuscular injection of meralluride does not enhance the diuretic response to the latter. Ethoxzolamide is a somewhat more potent diuretic agent than acetazolamide both on a weight basis of the compounds and from the standpoint of the maximum obtainable diuretic response. It is suggested that an action in addition to anhydrase inhibition may explain the difference. The average maximally effective dose of ethoxzolamide produces a diuretic effect about equivalent to that with approximately 0.7 cc. of intramuscularly given meralluride.

1300 York Ave. (21) (Dr. Gold).

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The ethoxzolamide used in this study was supplied as Cardrase by the Upjohn Company, Kalamazoo, Mich.

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RESULTS OF LONG-TERM USE OF TOLBUTAMIDE (ORINASE) IN DIABETES MELLITUS

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Factors favoring success with tolbutamide in the treatment of diabetes were sought in a study of 1,030 diabetic persons. There were 772 in whom it was deemed feasible to begin maintenance studies with tolbutamide alone. In 136 of these, trial indicated within a month that tolbutamide alone was inadequate (primary failure). In 407 patients in whom good control of hyperglycemia and glycosuria was obtained, important characteristics were that the onset of diabetes had usually occurred after the age of 40 years and that the insulin requirement was less than 20 units daily. In 40 patients results with tolbutamide became unsatisfactory after an earlier period of good control (secondary failure). A single-dose, four-hour response test was helpful in selection of patients for long-term maintenance therapy with the drug. There were only eight patients in whom the use of tolbutamide had to be stopped because of side-effects; the symptoms of toxicity were generally urticaria and minor digestive complaints. Histological examination of liver and pancreas was carried out in 2 of 12 patients who died of various causes during the period of observation; no evidence of damage attributable to the drug was obtained. Since tolbutamide is taken orally, it is especially welcome to patients handicapped by blindness or by other conditions which make self-injection difficult. It should not be used if dietary restriction alone will suffice or if tolbutamide is not effective and insulin is found necessary to provide good control.

Experience with sulfonylurea compounds in patients with diabetes began in the Joslin Clinic in December, 1955, with the use of carbutamide (BZ 55). Tolbutamide (Orinase) was used first in February, 1956. Experience here as elsewhere throughout the world has amply confirmed the blood sugar lowering effect of these agents, as found earlier in clinical trials in Germany.

Although Janbon [1] and Loubatières [2] and their co-workers as early as 1942 had described the hypoglycemic effect of certain sulfonamides and in the ensuing years continued to carry out studies with these compounds, Franke and Fuchs [3] were the first to use a related chemical agent, BZ 55, in the treatment of diabetes. Carbutamide (1-butyl-3-sulfonylurea) was subjected to fairly extensive clinical trial in the United States and Canada from late in 1955 until the fall of 1956, when it was withdrawn from use with patients because of a high incidence of toxic manifestations including allergic skin rashes, jaundice, leukopenia, thrombocytopenia, and agranulocytosis.[4] In addition to these untoward effects, carbutamide has the disadvantage that it is bacteriostatic, with some influence on the intestinal flora and the development of sulfonamide-resistant strains of bacteria in the body.[5]

Tolbutamide (1-butyl-3-*p*-tolylsulfonylurea), known first in Germany as D 860, Rastinon (Hoechst), or Artosin (Boehringer) [6] and in the United States as Orinase,[7] differs chemically from carbutamide only in having a methyl group substituted for the amino group in the para position on the benzene ring. This slight difference brings about three changes in properties: 1. Tolbutamide is not

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bacteriostatic. 2. In the same dosage, tolbutamide is not quite as hypoglycemic as carbutamide, probably due to its more rapid excretion.[8] 3. Tolbutamide so far has shown itself to be much less toxic than carbutamide.

In the present paper are summarized our results with the long-term use of tolbutamide. In addition, there will be outlined some guiding principles for the use of this drug.

Material and Methods

From February, 1956, until Nov. 10, 1957, we gave tolbutamide at one time or another to 1,030 patients with diabetes. The group comprised ambulatory patients seen at the Joslin Clinic, inpatients at the New England Deaconess Hospital, and summer campers at the Elliott P. Joslin and Clara Barton Birthplace Camps for diabetic children. Except for children and other selected persons given single-dose response tests and except for certain subjects chosen at random, particularly in the early months of the study, patients with whom the tolbutamide trials were carried out were in general those above the age of 40 years and those whose insulin requirement was below 40 units a day. The group studied was, therefore, a selected one, although no strict rules were followed in this regard.

Early in the study a sulfonylurea response test was devised in order to have some way of determining in advance those patients most likely to respond favorably to the drug in maintenance studies. The procedure used was as follows: 1. In adult patients with stable diabetes under control with small doses of insulin, omit insulin during the two days immediately preceding the test day. If the dose is 20 units or more daily or if omission of insulin seems potentially dangerous, give crystalline insulin in appropriate dosage during these two days. 2. On the day of the test, withhold insulin and food until the test has been completed. 3. Determine the blood sugar level with the patient in the fasting state. 4. Give (to adults) 3 Gm. of tolbutamide by mouth. 5. Determine the blood sugar level four hours after administration of the drug.

In the original interpretation[9] of findings during the response test, a satisfactory result was considered to have been secured if within four hours there was a fall in blood sugar level of more than 20% of the initial value. In a recent analysis of results, this was found not valid at all levels of initial blood sugar and so a change in criteria was made which will be discussed in the section entitled Sulfonylurea Response Test.

Various methods of establishing the dosage of tolbutamide were used. At first many patients were given 3 Gm. daily for one or two days, then 2 Gm. daily for one or two days, and finally a maintenance dose of usually 1 Gm. a day. More recently, patients found to be quite responsive to the drug in the test just described have been started at once on therapy of 1 Gm. daily, with success. In general, the entire dose has been given daily before breakfast. However, in some instances, particularly in those patients whose maintenance requirement proved to be more than 1 Gm. daily, the dose was divided by giving some of the drug before breakfast and some before supper, with the larger part before breakfast. This division of dosage is justified by a consideration of the length of time a given dose of tolbutamide provides an effective blood level of the drug, namely 8 to 10 hours. Relatively few patients complained of local gastric irritation after taking the drug; in these the tablets may be given satisfactorily with meals rather than on an empty stomach.

Early in the study it was found desirable to set up standards of control in order to have a uniform method of evaluating results. Consequently, satisfactory levels of blood sugar and amounts of sugar in the urine were arbitrarily chosen. These are given in table 1.

TABLE 1.—*Blood Sugar Levels and Amounts of Sugar in Urine Used as Standards of Control**

Relation to Food	Degree of Control†			
	Good		Fair	
	Blood Sugar, Mg./100 Cc.‡	Urine Sugar, %	Blood Sugar, Mg./100 Cc.‡	Urine Sugar, %
Fasting	110	Trace	130	0.1
1 hr. p.c.	150	0.3	180	0.5
2 hr. p.c.	130	0.1	150	0.3
2 hr. p.c.	110	Trace	130	0.1
Urine sugar in 24 hr.	2 Gm. or less		5 Gm. or less	

* For the purpose of classification as to degree of control, the majority of values must conform with the standards listed in the table. All others are considered poor.
† These standard values are the highest acceptable.
‡ "True" glucose as determined by the Somogyi-Nelson procedure.

In order for results to be regarded as "good" or "fair," respectively, it was required that the majority of the blood sugar values fall within the limits prescribed in table 1. An exception was made in those instances in which the trend in most recent tests was definitely toward poorer or better results, as the case might be. Blood sugar determinations were made on both capillary and venous blood with use of the Nelson modification[10] of the Somogyi procedure, which yields values for true glucose. These values average 20 to 25 mg. per 100 cc. lower than those obtained by Folin-Wu or comparable procedures. Sugar in urine was determined quantitatively by the Sumner-Exton method using di-nitro salicylic acid.[11]

Early in the studies, serial white blood cell counts were carried out but were later discontinued since no instance of leukopenia or agranulocytosis was encountered. Extensive studies of liver function were done throughout the period of tolbutamide administration; the results will be published in a separate paper.[12]

Careful adherence to diet was urged with all patients. The composition of the diets was the same as that with comparable patients treated with insulin and provided usually 150-200 Gm. of carbohydrate, 60-100 Gm. of protein, 60-100 Gm. of fat, and 1,400-2,100 calories daily. The body weight obtained at each examination of the patient often furnished a clue as to the probable degree of cooperation of the patient as regards diet.

Presentation of Data

In figure 1 is shown graphically the outcome of treatment of patients given tolbutamide. Of 1,030 patients who at one time or another were given the drug, 227 had the single-dose response test only; most of these were children in summer camps and the subjects of a special study, the results of which have been reported.[13] In addition, for 21 patients data were insufficient and 10 others were treated with both tolbutamide and insulin. Based on experience with the last-named group and with a larger number of patients treated for short periods of time with both tolbutamide and insulin, our impression is that little or nothing is to be gained by such combined treatment.

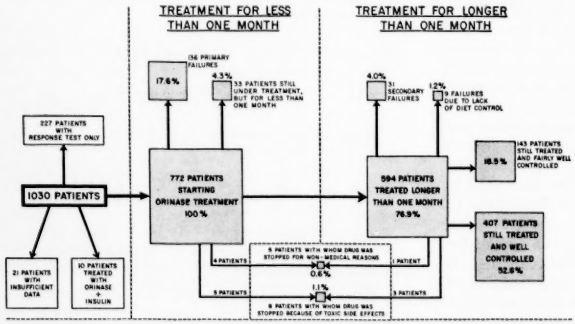
TREATMENT FOR LESS THAN ONE MONTH
TREATMENT FOR LONGER THAN ONE MONTH
136 PRIMARY FAILURES
17.6%
4.3%
33 PATIENTS STILL UNDER TREATMENT, BUT FOR LESS THAN ONE MONTH
4.0%
31 SECONDARY FAILURES
12%
9 FAILURES DUE TO LACK OF DIET CONTROL
227 PATIENTS WITH RESPONSE TEST ONLY
1030 PATIENTS
772 PATIENTS STARTING ORINASE TREATMENT 100%
594 PATIENTS TREATED LONGER THAN ONE MONTH 76.9%
143 PATIENTS STILL TREATED AND FAIRLY WELL CONTROLLED
18.5%
407 PATIENTS STILL TREATED AND WELL CONTROLLED 52.6%
21 PATIENTS WITH INSUFFICIENT DATA
10 PATIENTS TREATED WITH ORINASE + INSULIN
4 PATIENTS
9 PATIENTS WITH WHOM DRUG WAS STOPPED FOR NON-MEDICAL REASONS
0.6%
1 PATIENT
1.1%
9 PATIENTS
3 PATIENTS
8 PATIENTS WITH WHOM DRUG WAS STOPPED BECAUSE OF TOXIC SIDE EFFECTS

Fig. 1.—Outcome of treatment in 772 selected patients given tolbutamide.

After elimination of the above-mentioned groups, 772 patients were left on whom maintenance studies were actually begun with tolbutamide alone. With 136 (17.6%) of these, the result was a "primary failure," i. e., within one month it became apparent that blood and urine sugar values were sufficiently abnormal to demand the classification of a "poor" result (table 1). It must be admitted that in a certain few of these patients the treatment has been continued for periods beyond one month at the patient's insistence, or with the hope of eventual success, or because of compelling reasons such as blindness of the patient.

As indicated in figure 1, there were an additional 33 patients, or 4.3% of the total of 772, whose response to treatment has been satisfactory but who have been excluded from further consideration because the total length of treatment at the time of conclusion of the study was less than one month.

Among the total of 772 patients were 8 in whom the drug was discontinued because of side-effects consisting of transient allergic dermatitis, jaundice (one case in a patient with cirrhosis of the liver), and mild digestive disturbances. In an additional five patients the treatment was discontinued for nonmedical reasons. The side-effects will be discussed in more detail later in the paper.

With the above exclusions, 594 patients, or 76.9% of the total, were left for consideration. These patients received tolbutamide for periods ranging from 1 to 20 months (table 2). Of these, good control of blood and urine sugar levels was obtained in 407 patients (52.6% of the total of 772 patients) and fair control in 143 patients (18.5% of the 772 subjects). Thus, of the total of 772 patients, 71.1% responded satisfactorily during long periods of maintenance therapy with tolbutamide. With a few exceptions, such as those who have died intercurrently and those who are now treated with a restricted diet alone, these patients are still receiving the drug.

As is evident from figure 1, 31 patients who originally responded satisfactorily to tolbutamide later did not do so. The cause of these "secondary failures" is not clear and will be discussed later. However, in nine additional patients the secondary failure seemed almost surely due to increasing negligence of the patient as regards diet. Such lack of adherence to diet was usually reflected in significant gain in body weight. These two groups combined gave a total of 40, or 5.2%, secondary failures.

Side-effects.—Because of untoward effects encountered with carbutamide (BZ 55), early in the experience with tolbutamide fear was expressed that use of the drug would be limited by toxic side-effects. However, results to date indicate that the incidence of untoward effects is extremely low. The chief problem, therefore, is not toxicity of tolbutamide but rather the harmful effects of uncontrolled diabetes in patients unwisely chosen for tolbutamide treatment.

Figure 1 lists 8 (1.1%) of the 772 patients in whom tolbutamide treatment was discontinued because of toxic side-effects. In four of these, allergic skin rashes developed. In three others, the treatment was stopped because the patients complained variously of itching of the face, heartburn, chills, epigastric pain, nausea, or acid regurgitation. The

symptoms were mild and of questionable relation to the drug therapy. In one patient with cirrhosis of the liver, esophageal varices, and hepatosplenomegaly, jaundice occurred three months after beginning tolbutamide therapy. It is difficult in this patient with serious liver disease to decide whether the jaundice was due to the drug; this problem is discussed in greater detail elsewhere.[12]

Fatal Cases.—During the period of observation 12 patients died who had received tolbutamide for varying periods of time. Among these, the cause of death was myocardial infarction in seven cases. One death was reported from each of the following causes: acute congestive heart failure; probable cancer, site not known; possible diabetic coma; cerebral thrombosis; and fracture of thigh. In only two instances was a postmortem examination carried out. A 69-year-old man who had diabetes of almost 16 years' duration died of myocardial infarction after having received tolbutamide for five and one-half months. A 78-year-old man with diabetes of four and one-half months' duration died of acute congestive heart failure after having received tolbutamide for four months. On histological examination, in neither case did the pancreas show any evidence of damage to the alpha or beta cells nor did the liver show any changes which might be attributed to the drug.

The patient who was reported to have died in diabetic coma was a 73-year-old man with diabetes of 18 years' duration. Tolbutamide therapy had been started on April 10, 1956, while he was at the New England Deaconess Hospital for treatment of cancer of the prostate. On June 21 he was transferred to another hospital for prolonged care and we did not see him again. At that time a blood sugar value of 92 mg. per 100 cc. was obtained. The diabetic condition appeared under excellent control with 0.5 Gm. of tolbutamide daily. He remained in the other hospital for over four months and was said during this time to have received 0.5 Gm. of tolbutamide daily. It was stated that, although on Nov. 16 a blood sugar value of 280 mg. was obtained, he was allowed to go home on a regimen of the same dosage of tolbutamide. However, readmission to the other hospital was necessary on Nov. 19 because of nausea and vomiting. It was stated that the patient had not taken tolbutamide and had eaten without regard to diet restrictions while at home. He was reported to have been in diabetic ketoacidosis; he was given 50 units of insulin, but died. No postmortem examination was carried out.

Factors Influencing Results of Tolbutamide Treatment

Age at Onset of Diabetes.—In figure 2 is shown the relation of age at onset of diabetes to the results secured with tolbutamide. It is noteworthy that, in the first three decades, there were relatively more failures than successes, as might have been predicted. In the decades 30-39.9 and 40-49.9 years, the ratio of number of patients with good results to those with primary failure was roughly 2:1. In succeeding decades, the ratio between good results and failures increased progressively. It must be kept in mind that the figure gives good results on selected patients. Tolbutamide trials were carried out much less commonly in patients below the age of 40 years than in those in older age groups.

Age of Patient at Time Tolbutamide Therapy Was Started.—It is evident from figure 3 that the number of patients with good and fair responses in the various age groups was relatively the same as those in whom primary and secondary failures were obtained. Therefore, the age of the patient at the time tolbutamide therapy was started is not of fundamental importance when one is dealing with subjects who are over 40 or 50 years of age. The important factor, as has just been brought out, is the age of the patient at the time diabetes had its onset, since in general the sulfonylurea compounds are effective in maturity-onset but not in growth-onset diabetes.

Duration of Diabetes at the Time Tolbutamide Therapy Was Started.—In figure 4 are shown the results of tolbutamide maintenance trials tabulated as to duration of diabetes. Two significant facts emerge: 1. The percentage of primary failures increased with increasing duration of diabetes. 2. Despite this trend, a significant number of patients with diabetes of 10 or more years' duration responded favorably. After consideration of these data with those shown in figure 2, it is reasonable to suppose that the successes in patients with long-term diabetes were, by and large, in those with onset above 40 years of age. Nevertheless, in this connection it is worthwhile to point out that, in dealing with subjects with maturity-onset type of diabetes, duration of diabetes need not be a contraindication to success with the orally given agent.

TABLE 2.—*Duration of Treatment in 594 Patients on Tolbutamide Therapy for Longer Than One Month**

Result of Treatment	Patients Receiving Tolbutamide for Number of Months Indicated†																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	Total
Good control	26	43	54	46	36	37	21	12	21	24	18	18	10	12	10	5	5	5	1	3	407
Fair control	7	14	7	15	15	19	9	7	6	4	8	15	4	2	1	2	6	1	1	...	143
Secondary failures	5	3	7	5	5	...	2	2	2	...	...	...	...	...	...	...	...	...	...	...	31
Diet failures	1	1	...	1	...	...	...	...	3	...	1	1	...	1	...	...	...	...	...	...	9

* Not tabulated are 4 patients with whom, after one month of treatment, tolbutamide was discontinued (in 3 patients because of side-effects and in 1 for a nonmedical reason).

† 1=1-1.9 months; 2=2.9 months; etc.

Insulin Dosage Prior to Tolbutamide Treatment.—The influence of the prior insulin dosage on the outcome of treatment with tolbutamide is shown in figure 5. As might have been anticipated, successes were much more common in those patients whose insulin dosage was smallest, and particularly in those formerly receiving less than 20 units daily. Contrariwise, the relative number of failures rose as the insulin dosage increased. In this connection it is important to make a distinction between insulin dosage and insulin requirement. One knows what the patient's insulin dose was, but it is not easy in retrospect to state just what the true insulin requirement or deficit was. In figure 5, among those patients tabulated as receiving no insulin were many with newly discovered diabetes who had never taken insulin and yet actually had an insulin requirement. As is evident from the figure, some of these responded satisfactorily to tolbutamide treatment and others, presumably those with larger insulin requirements, proved to be primary failures.

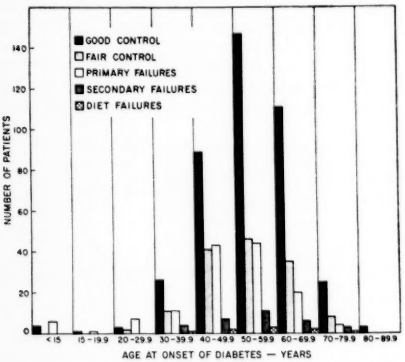

Fig. 2.—Correlation of age of patient at onset of diabetes with outcome of treatment with tolbutamide.

Duration of Insulin Treatment Prior to Use of Tolbutamide.—The results shown in figure 6 show that the relative percentage of failures, primary and secondary, rose progressively with duration of prior insulin treatment. This may have been due in part to the inclusion of relatively more patients with growth-onset type of diabetes in the groups with long-term insulin treatment. Nevertheless, as is evident from figure 6, treatment over 5, 10, or more years with insulin is not necessarily a contraindication to success with tolbutamide.

Sex.—As shown in table 3, of the 726 patients suitable for analysis, 315 were males and 411 females. There was a definitely higher incidence of failures, both primary and secondary, among females than males. Since the cause for this was not immediately apparent, a study was carried out to evaluate factors which might have had a bearing on the results obtained. Of the various items, one with which some relationship appeared to exist was the previous insulin requirement which happened to be appreciably higher among the females than the males, thus creating less favorable conditions for the action of the sulfonylurea compound. In addition, it may be of significance that, among the nine patients with secondary failures probably due to diet laxity, seven were females.

TABLE 3.—*Sex Distribution of 726 Patients Receiving Tolbutamide*

Result of Treatment	Males No.	Males %	Females No.	Females %
Good control	196	62.2	211	51.4
Fair control	64	20.3	79	19.2
Primary failures	43	13.7	93	22.6
Secondary failures	10	3.2	21	5.1
Diet failures	2	0.6	7	1.7
	315	100.0	411	100.0

Body Weight.—The body weight at any given time may not reflect accurately the constitutional type of the individual, and the latter may be more closely related to the response to tolbutamide than the body weight itself. Although data in this regard are incomplete, it is our impression that patients who are overweight are more likely to respond favorably to tolbutamide. It must be recognized, however, that if an obese patient follows a restricted diet and loses weight while taking medicaments orally, the beneficial effect on the diabetes may be due to dietary restriction and loss of weight rather than to the drug.

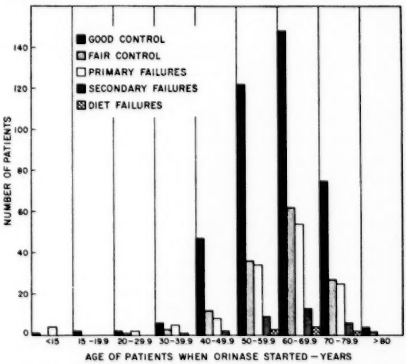

Fig. 3.—Correlation of age of patient at time tolbutamide treatment was started with outcome of treatment.

Sulfonylurea Response Test

Mention has been made earlier in the paper of the sulfonylurea response test, which has been used in the selection of patients as regards probable suc-

cess or failure in the use of the drug. In all, some 500 such response tests were carried out. In figure 7 the results in 409 of these are shown, the initial (fasting) blood sugar level having been plotted

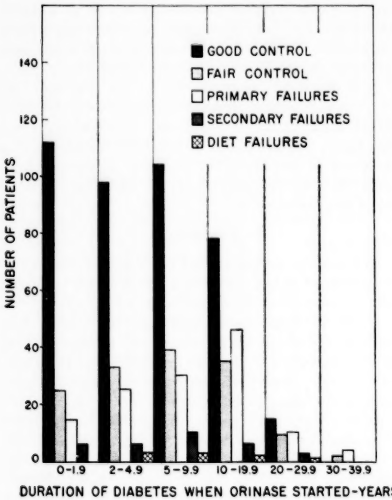

Fig. 4.—Correlation of duration of diabetes at time tolbutamide treatment was started with outcome of treatment.

against the percentage fall in blood sugar level in two to four hours after the giving of the test dose of the drug.

The data shown are those obtained with patients who later were found to have good control, those with fair control, and those with primary and secondary failures. As is seen, our former standard [9] of more than 20% fall in blood sugar level as predicting a satisfactory result on maintenance studies is not strictly valid. In those patients in whom the initial blood sugar level was more than 120 mg. per

TABLE 4.—*Correlation Between Fasting Blood Sugar Levels and Decrease After Tolbutamide Necessary to Predict Success in Treatment*

Fasting Blood Sugar Level, Mg. per 100 Cc.	Fall in 4 Hr. Required to Predict Satisfactory Maintenance Result, %
120	20
140	30
160	40
200	50
250	60

100 cc., there were later many failures despite a fall of more than 20% in the one-dose response test. Table 4 has been devised to bring out the rough correlation found in figure 7. It should be added that in those patients with a fasting blood sugar level of 100 mg. per 100 cc. or less, the fall in blood sugar level may be less than 20%, and yet such patients, if adults, may respond well to the drug in maintenance studies.

Two points regarding the sulfonylurea response test are worthy of emphasis. First, the level of the initial (fasting) blood sugar is in itself of great importance. A successful outcome of maintenance on tolbutamide therapy is much more likely to occur in those patients with a fasting blood sugar level of, say 150 mg. per 100 cc., than those with a value of 300 mg. per 100 cc. Second, it will be noted, with use of the sliding scale of percentages given in table 4, that at each level of fasting blood sugar the percentage of fall required for a satisfactory result is that which will lower the blood sugar to a normal level. In other words, one may define a satisfactory sulfonylurea response test simply as one in which the single dose of the drug lowers the

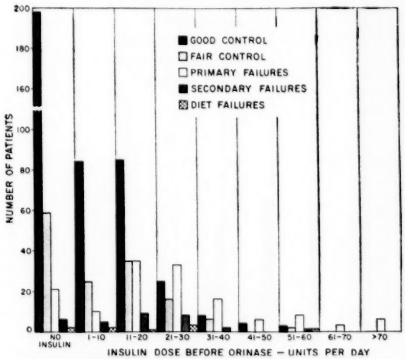

Fig. 5.—Correlation of insulin dosage prior to use of tolbutamide with outcome of treatment.

blood sugar level to normal in the space of a few hours. We have chosen four hours as the length of time in which to carry out the test, since in most instances the major part of the blood sugar fall has taken place in that time and since the test can be completed in the course of a forenoon. However, in some instances the full effect of the drug is not seen until later, say six or eight hours after administration. It is likely that this situation accounts for the discrepancy between the results of the sulfonylurea response test and those of maintenance studies in those patients who showed an unsatisfactory fall during the response test and yet achieved good control of blood sugar when treatment was maintained over weeks of time.

It may be calculated from figure 7 that about one-fourth of the patients who later achieved good control (62 of 240) had response tests earlier which

would be classified as unsatisfactory with respect to table 4. Consequently, it may properly be said that the sulfonylurea response test is only partly reliable in predicting good maintenance results. However, examination of figure 7 in the same way shows that, of 74 patients with primary failures, only 5 had satisfactory response tests in spite of the fact that many more than 5 had met the usual criteria for probable success with tolbutamide, such as older age at onset of diabetes and low insulin requirement. It is instructive that, among 70 patients who achieved fair control, about half (36) had sulfonylurea response tests earlier which were satisfactory and the other half unsatisfactory, thus taking a middle position between the well-controlled cases and the primary failures. Among 25 patients with

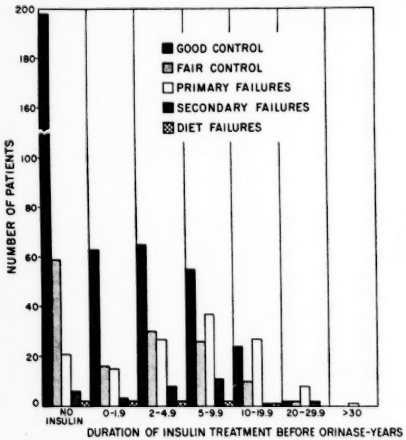

Fig. 6.—Correlation of duration of insulin therapy prior to use of tolbutamide with outcome of treatment with orally given agent.

secondary failures in whom response tests had been done earlier, 14 had had satisfactory and 11 unsatisfactory results with the response test.

In summary, the sulfonylurea response test affords a helpful, although by no means infallible, guide in the selection of patients most likely to respond favorably to drug therapy in day-by-day usage, gives enough security to start the treatment with nonhospitalized patients, and excludes cases in which it would be dangerous to stop treatment with insulin even for a few days. The test is quite reliable in predicting "primary failures," thereby avoiding the use of the drug in unsuitable patients. Moreover, a negative result has often helped to convince doubting patients that they cannot be treated successfully with tolbutamide. It is not as helpful in predicting "secondary failures," i. e., late failures in those patients who at first achieve good control.

If the results of the sulfonylurea response test are borderline or if on clinical grounds it seems reasonable to predict success on maintenance therapy, one may make a trial of day-by-day treatment. However, the patient should be kept under close supervision, with frequent tests of urine sugar and periodic determinations of the blood sugar level.

It is our custom on the day of the response test to have the patient, if an outpatient, wait until the blood sugar results are known. If the findings are favorable, a treatment schedule with tolbutamide is outlined; if unfavorable, insulin, if indicated, is given before the patient leaves and future treatment is planned.

Comment

The results just presented are those of a study of the effect of tolbutamide in 1,030 diabetic patients. After elimination of those with single dose tests only, those with insufficient data and those few treated with both tolbutamide and insulin, a total of 772 patients were left for consideration. Of these, 143 (17.6%) had "primary failures" with tolbutamide and consequent indication for treatment with insulin. Other small groups of patients having been discarded for various reasons, 594 patients were left for long-term study. It must be emphasized that, by this time, this group had become a rather highly selected one composed almost entirely of middle-aged and elderly persons with maturity-onset type of diabetes and with prior daily insulin dosage usually of 20 units or less. Among these 594 patients, long-term maintenance on tolbutamide therapy of 1 to 20 months resulted in good control of diabetes in 407 patients and in fair control in 143 patients.

From time to time, workers have reported as to the percentage of diabetic patients in whom hyperglycemia and glycosuria may be controlled with tolbutamide. Such percentages have meaning only when a statement is made as to the selection of patients used for tolbutamide trial. Although in selected groups of patients success may be achieved to an extent as great as 60 to 80% of subjects, if one considers all diabetic patients, a much lower percentage of the total can be treated successfully with the orally given agent.

It must be pointed out that, in the present study, the standards arbitrarily chosen for "good" and "fair" control are relatively strict as compared to those used commonly for patients maintained on insulin therapy. However, it has been our belief that, since the main advantage of the orally given hypoglycemic agents is that of convenience to the patient, truly good control should be insisted on if this type of treatment is to be followed instead of that with insulin. The hazard of hypoglycemia often prevents attempts at rigid control of diabetes with insulin. With tolbutamide, since significant and

symptomatic hypoglycemia is rare, one can aim for normal blood sugar values without fear of undue depression of the blood sugar. Finally, analysis of data shows conclusively that, with respect to factors such as older age at onset of diabetes and lower insulin requirement as well as a satisfactory sulfonylurea response test, the patients who achieve good control are in a quite different class than those with fair control. This also lends weight to the feeling that probably tolbutamide therapy should not be continued for long periods in patients for whom only fair control can be achieved.

Indications for Tolbutamide Therapy.—It has been the experience of workers everywhere, beginning with the reports of German clinicians [14] as early as 1955, that the sulfonylurea compounds are effective in some middle-aged and elderly diabetic persons with a low insulin requirement. They are not effective in ketoacidosis and coma, during infections, or during and after many major surgical operations. They are not effective in children or in adults with the juvenile, unstable type of diabetes with an easy tendency to acidosis. Our experience agrees with these findings. The chief problem has been to attempt to find simple and workable criteria by which success or failure may be predicted among middle-aged and elderly persons with "mild" diabetes.

Analysis of our data indicates that success with tolbutamide in control of hyperglycemia and glycosuria is favored most in cases of maturity-onset type of diabetes and in cases of low insulin requirement. In other words, the drug works best in middle-aged and elderly diabetics who otherwise would take relatively small doses of insulin. Other favoring influences, discussed above, are short duration of diabetes and of insulin treatment; these are probably indirect factors.[14b] The sulfonylurea response test, already described, is also helpful in selecting patients in whom diabetes is likely to be controlled with tolbutamide therapy, provided a sliding scale of percentage fall in blood sugar level is employed.

Secondary Failures.—If the above considerations are kept in mind in choosing patients for tolbutamide therapy, there should be only a relatively small number of primary failures. However, the problem of "secondary" failures remains, i. e., the situation in which initial success in treatment over a period of at least one month is followed by "escape" from the effect of the drug with increase in hyperglycemia and glycosuria. Despite the fact that in our studies strict standards of control were used, a small number of secondary failures (including those due to lack of diet control) occurred—40, or 5.2% of the total. It must be acknowledged that further experience over a longer period of time may show a change in this regard.

The cause of the secondary failures is obscure. Critical analysis of results in our series of patients does not suggest that the cause was poor selection of patients or use of the wrong indications.[14b] In fact, in at least two-thirds of the patients with secondary failures, the influencing factors, such as results of the sulfonylurea response test, age at onset of diabetes, and the insulin dose, were the same as in those patients who have continued to the present to have satisfactory control with tolbutamide.

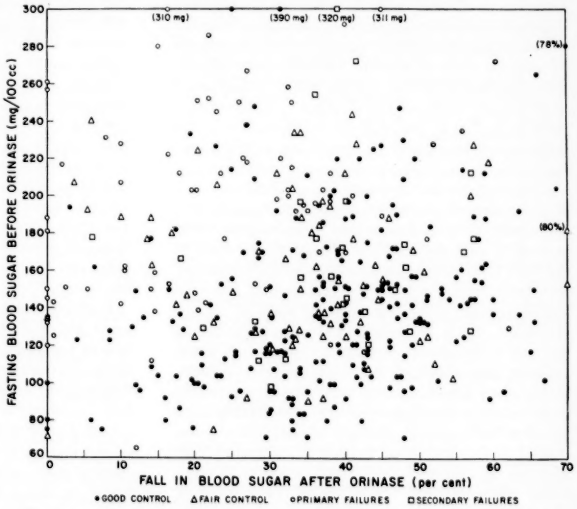

Fig. 7.—Correlation of fall in blood sugar level after single dose of tolbutamide and initial level of blood sugar with results of long-term treatment.

It has been suggested that in such patients a decreased capability for production of endogenous insulin has been brought about by prolonged stimulation with tolbutamide. As evidence in favor of such a view, some have reported [14b] that occasionally, on returning such patients to insulin therapy, the requirement has been significantly greater than before tolbutamide treatment. However, such has not been the experience in our patients. With the occurrence of secondary failures and return of patients to insulin therapy, the requirement has remained about the same as before. It must be

pointed out that, in a situation such as this, the requirement for insulin after a period of poor control on tolbutamide therapy may well be somewhat higher than that in the same patient a few weeks later after a period of good control with insulin. Furthermore, entirely apart from tolbutamide, patients maintained on insulin therapy over extended periods of time often experience significant changes in insulin requirement.

Influence of Diet.—It should be emphasized that certain of the so-called failures with tolbutamide are in reality due to failure of the patient to follow diet instructions. Lack of adherence to diet affects, of course, the results of treatment with insulin, but with tolbutamide other considerations are evident. Some patients receiving medication orally instead of by injection may not be so impressed with the existence of diabetes and the necessity of following a diet. Furthermore, dietary indiscretions may be counterbalanced to some extent by administration of a larger dose of insulin, whereas with tolbutamide increase in dosage will not allow an increased food intake. Regardless of other considerations, there is no doubt but that the introduction of the orally given hypoglycemic agents has called attention anew to the fundamental and striking value of a restricted diet in the treatment of diabetes.

An occasional patient receiving tolbutamide may experience such an increase in carbohydrate tolerance that, with reduction in dosage of the drug to only 0.5 Gm. daily, the urine remains consistently free from sugar and blood sugar values are well within normal limits regardless of time of day or relation to meals. In such patients, the indication is to omit tolbutamide entirely. In certain of these patients, one will find that even without tolbutamide, normoglycemia and aglycosuria persist. In such instances doubt may be raised justifiably as to whether tolbutamide therapy should have been started in the first place. Indeed, this situation emphasizes the point that patients with "mild" diabetes, particularly if obese, should be treated at first with diet restriction alone, since in many cases remarkable improvement may be expected. However, it would appear likely that many patients at first require and benefit from tolbutamide, in addition to diet restriction, and improve after a period of time so that the drug is not necessary later. In these patients, however, it may be necessary at a later date to return to tolbutamide therapy.

Special Advantages of Oral Treatment.—The chief advantage of the orally given hypoglycemic agent is that of convenience. Consequently, in any patient in whom the indications for such management are questionable or in whom the results after trial of the orally given compound are poor, insulin should be used without hesitation and without delay. However, the convenience of treatment by mouth as opposed to treatment by injection appeals to all persons. It is particularly welcome to blind patients, to those with disabilities or tremor of the hands, and to those who are highly nervous. In this connection, there should be recorded our experience that many patients "feel much better" on therapy with tolbutamide than with insulin. This impression is, of course, greatly influenced by emotional factors such as relief from the necessity of injections and freedom from worry regarding insulin (hypoglycemic) reactions. One must confess that at times such patients may return for examination with significant hyperglycemia and glycosuria, with lack of correlation with degree of control of diabetes and sense of well-being. This experience emphasizes that patients receiving tolbutamide must be seen regularly and blood sugar determinations done at sufficiently frequent intervals to insure that the diabetes is kept under good control.

One might postulate a special benefit in those who are allergic to insulin. However, tolbutamide treatment is not successful in many such patients because of the nature of the diabetic state and a high insulin requirement. Furthermore, even in those in whom tolbutamide treatment yields satisfactory results, one must keep in mind the possible need for insulin in the future at times of emergency. Certainly if in any given patient such seems at all likely, it is wise to carry out desensitization to insulin and to use insulin rather than tolbutamide in treatment.

Hypoglycemia.—In addition to convenience, treatment with tolbutamide has the added advantage of almost complete freedom from significant hypoglycemia. In our series of well over 1,000 patients given tolbutamide at one time or another, in only a very few instances was symptomatic hypoglycemia recognized, despite the fact that most adult patients at the start were given a full dose of 3 Gm. in the fasting state, with food being withheld for four hours in order to carry out the tolbutamide response test. The case of one patient with symptomatic hypoglycemia is given below.

A thin, frail woman, 74 years of age, with diabetes of eight years' duration had been admitted to the hospital after a cerebral thrombosis with right-sided hemiparesis. Since discovery of diabetes she had taken a small dose of insulin daily; most recently this had been 8 units of the protamine zinc type daily before breakfast. On Aug. 8, 1957, a sulfonylurea response test was carried out after a day during which no insulin had been given. The fasting blood sugar level was 83 mg. per 100 cc. After 3 Gm. of tolbutamide was administered, the blood sugar level in two hours had fallen to 68 mg., and in four hours to 50 mg. per 100 cc. During most of the day the patient complained of malaise and appeared a bit dull. However, symptoms were mild and she carried through the day without particular incident. The following morning there was difficulty in arousing her. Hypoglycemia was suspected and blood drawn for sugar

determination. After this, she was given orange juice with some difficulty and she promptly revived. When the blood sugar value was reported it was stated to be 38 mg. per 100 cc. She was placed on therapy of 0.5-1.0 Gm. of tolbutamide daily, and in February, 1958, at a hospital stay her diabetic condition was found to be under excellent control.

The incidence of marked, prolonged, or symptomatic hypoglycemia after treatment with tolbutamide has been so low that we believe hospitalization is not necessary for initiation of treatment, even on the test day on which a full dose of 3 Gm. is given at one time. Furthermore, the almost entire freedom from danger of hypoglycemia, particularly on maintenance doses of 0.5 to 2.0 Gm. of tolbutamide, may make it possible for patients to engage in those occupations in which potential hypoglycemia has been considered disqualifying.

Summary

Tolbutamide (Orinase) was used in treatment of 1,030 diabetic patients. In 772 of these, treatment with tolbutamide was begun and, at the time of completion of the study, had been carried out for 1 to 20 months in 594 patients. Good control of hyperglycemia and glycosuria was obtained in 407 (52.6%) and fair control in 143 (18.5%) of this selected group of 772 patients. The incidence of failures was as follows: "primary," i. e., within the first month of treatment, 136 patients (17.6%); "secondary," 31 patients (4%); failures due to disregard of diet, 9 patients (1.2%). In 33 patients (4.3%) the drug had been used for less than one month; in 8 (1.1%) treatment with tolbutamide was stopped because of toxic side-effects; and in 5 (0.6%) the treatment was discontinued for nonmedical reasons.

Factors favoring success with tolbutamide were primarily maturity-onset type of diabetes (onset usually above the age of 40 years) and a low insulin requirement (less than 20 units daily). A single-dose, four-hour sulfonylurea response test was found to be of value in pointing out those patients in whom primary failure with tolbutamide therapy is likely to occur.

Untoward effects were low in incidence and in general consisted chiefly of urticaria and minor digestive disturbances. In one patient with cirrhosis of the liver, jaundice occurred three months after beginning treatment with tolbutamide; the relation of jaundice to the drug is uncertain. In two patients dying of causes unrelated to tolbutamide administration, histological examination revealed no evidence of damage to the pancreas or liver which could be attributed to the drug.

In the selection of patients to be treated with tolbutamide, care should be taken to avoid, on the one hand, unnecessary use in those with whom dietary restriction will suffice and, on the other hand, unwise use in those requiring insulin for maintenance of control of diabetes.

15 Joslin Rd. (15) (Dr. Marble).

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MEDIAL TIBIAL MALLEOLUS
USE OF HOOKPLATE FOR FIXATION OF UNUNITED

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Nonunion of the medial tibial malleolus is one of a group of fractures for which there is no satisfactory method of internal fixation. Most of the difficulties can be overcome by the use of the hookplate here described. Made of malleable stainless steel in several sizes, it can be adapted closely to the contours of the bone structure. The hookplate fixation has been successfully used in over 350 cases representing fractures of the medial or lateral malleolus, comminuted or malunited malleolar fractures, olecranon fractures, especially if they were comminuted, and fractures in several other locations in the body. Usually these fractures represent a part of a joint, which is of great importance for structural stability and/or attachments of ligaments and tendons. In applying it, care is taken to preserve the articular surface of the bone and to achieve, if possible, a stable hairline reduction of the malleolar fragment so as to restore the normal ankle mortise. Also, the hookplate fixation allows a type of bone grafting procedure described and illustrated in this paper, which is technically not difficult. Ten fractures, one of which is described in some detail, have been treated with excellent anatomic and functional results.

The surgical treatment of nonunion of the medial tibial malleolus still presents a technical problem which has been given only scant consideration in literature and textbooks.[1] It is simply stated that in case of nonunion the fracture site should be freshened, a screw or wire should be used for fixation, and some type of bone graft should be applied.

Kelikian [2] describes a slightly different method in which an intramedullary bone graft is used and fixation obtained with two wire sutures. It is felt that these methods lack the degree of fixation for the small fragment which is desirable in order to obtain consistently good results. Therefore, a method is suggested which has been successfully applied in 10 cases of nonunion of the medial malleolus.

Principles of the Method

Fixation is obtained by means of a hookplate (fig. 1), commercially available in different sizes, which can be applied without any technical difficulty and which permits associated intramedullary or other types of bone grafting. The hookplates are of stainless steel, malleable, and can readily be shaped to conform to bony contours.

In the German literature, several authors [3] report favorably on the use of the hookplate. Lange [4] enumerates the different methods for fixation of the fractured medial malleolus and summarizes the advantages with the use of the hookplate. He states that the two hooks grasp the fragment firmly, eliminate the displacing force transmitted through the deltoid ligament, and provide reliable fixation to the tibia. Witt [5] stressed the same points in discussing the treatment of the fractured medial malleolus as either a fresh fracture or a pseudarthrosis.

It should be emphasized that not all patients with nonunion of the medial malleolus need surgical repair. In one group either the condition is asymptomatic and requires no treatment, or the fracture can be controlled by conservative measures or simple excision of the distal malleolar tip. It is the second group which usually experiences a progressive amount of pain on physical activity and requires reconstructive surgery.

In the typical case of nonunion of the medial malleolus, we find on the roentgenogram a rarefied line of bone defect surrounded by some sclerotic bone. The blood supply of the distal fragment depends on the level of the fracture. If it is a typical inversion type of fracture, evidenced by an oblique fracture line extending proximally toward the tibial shaft, the main blood supply to the fragment through the anterior tibial artery may still be intact. If it is the transverse type of fracture line (eversion type) at the level of the tibial joint surface or distal to it, this main blood supply is interrupted and the only vessels which remain are those reaching the fragment through ligamentous structures. This important aspect of the blood supply, which has been stressed by Kelikian, should be remembered at the time of surgery and preserved accordingly. Our aim is to reduce the fracture as exactly as possible after excision of the area of pseudarthrosis, retain all possible blood supply, obtain rigid fixation, and apply some type of bone graft.

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Surgical Procedure

The skin incision and subperiosteal exposure of the pseudarthrosis are performed in routine manner, extending proximally on the tibia sufficiently to

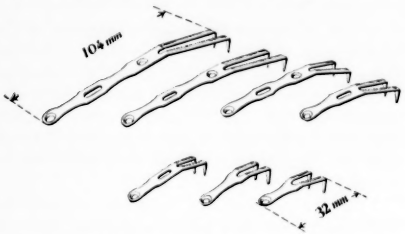

Fig. 1.—Hookplates from 32 to 104 mm. in length. Smaller ones have only one hole, whereas larger ones have two or three holes, one of which is enlarged to a slot to permit further impaction before screw is tightened.

allow the placement of the hookplate. The pseudarthrosis is excised, and the fragments are freshened down to cancellous bone. If the distal fragment is sclerotic, one will be unable to expose cancellous bone and must be satisfied with less suitable bone structure. Precaution is taken to preserve the articular surface. An attempt should be made to obtain a hairline reduction of the malleolar fragment to restore the normal ankle mortise. Occasionally, a portion of the anterior and posterior ligamentous attachments have to be severed, and the heel must be adducted to allow an accurate reduction. The main portion of the deltoid ligament, however, must be preserved.

By means of a Kirschner wire, two holes are drilled into or close to the tip of the malleolus. The holes are directed obliquely toward the fracture site (fig. 2, *A* and *B*) and are about 8 to 12 mm. apart, depending on the size of the malleolar fragment. The drill holes should not enter the joint and should remain inside the cancellous portion of the bone. A two-hole or three-hole hookplate is selected, depending on the size of the fragment and the force which is required to maintain reduction. In order to obtain maximum stability, a three-hole hookplate is preferred. This is in contrast to fresh fractures, which usually require only a small one-hole hookplate 32 mm. in length.

The hookplate and its prongs are bent with small pliers to conform to the bony contours of the fracture site, after which the hooks are introduced into the prepared holes and lightly impacted. Final adjustment of the shape of the hookplate can be made before the hooks are fully impacted. While the fracture is held tightly reduced by an assistant, with close contact of the hookplate to the bone, the first drill hole is made through both tibial cortices at the proximal end of the slot, followed by introduction of the screw. Prior to tightening of this screw, the fragment is again snugly approximated by the assistant. A screw is then inserted through the distal hole of the plate penetrating only one cortex in order to avoid the joint. Finally, the second bicortical screw is applied through the proximal hole in the plate. This completes the first part of the procedure and results in solid fixation of the fragment.

The second step is the bone grafting procedure. The following method has been found to be simple and rewarding. Directly behind the posterior prong of the hookplate and in front of the anterior prong, grooves 6 to 8 mm. in width and 15 to 20 mm. in length are made in the cortex of the tibial shaft.

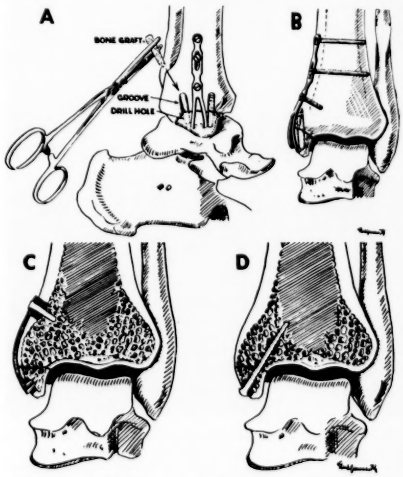

Fig. 2.—*A* and *B*, surgical procedure for nonunion of medial malleolus, illustrating solid fixation obtained with hookplate and bone grafting by cortical and cancellous pegs from wing of ilium. *C*, principle of hookplate fixation. Fragment is grasped by two hooks while screw rests securely against cortical type of bone in transverse direction to force of distraction. Screw and hooks are directed slightly towards fracture site in order to obtain firm grasping force. *D*, method of direct screw fixation in which screw engages only cancellous bone and in line of force distraction.

With these grooves as guides, drill holes are then made into the malleolar fragment (fig. 2). Two cancellous-cortical bone grafts of appropriate size to fit the drill holes are obtained from the wing of the ilium. These are introduced obliquely into the

two holes and are then impacted into the grooves. Additional cancellous material is used to fill the space around the grafts. If necessary, further grafting can be accomplished by a bone onlay over the fracture site. The wound is closed in layers beginning with the periosteum, and a long leg plaster is applied.

Postoperative Care

The plaster is changed after 14 days, and the sutures are removed. At the end of six weeks, a short leg plaster is applied until bone healing is demonstrated by roentgenogram. This usually occurs on an average of eight weeks after the operation. Foot and ankle exercises are begun at this time. Graduated weight bearing is started at 10 weeks, but full weight bearing is not permitted for an additional 2 weeks. Ten patients have been treated by this method. The following case is representative.

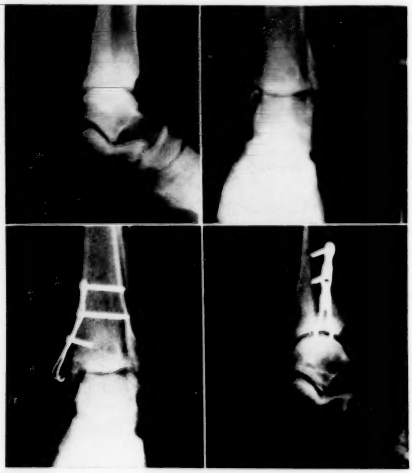

Fig. 3.—*Above*, anteroposterior and lateral roentgenograms of typical nonunion of medial malleolus 21 months after injury. *Below*, bony union 10 weeks after combined hookplate and bone grafting procedure.

Report of a Case

This patient, aged 20, fractured his medial malleolus in January, 1955. He was treated by closed reduction and immobilization in plaster. He was returned to duty about 10 weeks later with a definite nonunion. On Oct. 22, 1956, he twisted the same ankle severely while playing football and immediately developed pain over the old fracture site. It was decided, because of the patient's youth and desire for full athletic activity, to operate in order to obtain bone union. On Nov. 1, 1956, the patient was operated on by the method described above. There was eight weeks of postoperative immobilization followed by graduated weight bearing two weeks later. This patient was returned to duty on Jan. 23, 1957, 12 weeks after surgery, with no discomfort and with roentgenographic evidence of bone union (fig. 3).

Salient Points of the Method

1. The hookplate gives solid fixation of the fractured medial malleolus, regardless of size and shape. Screws and wires still allow distraction and rotation of the fragment if not well engaged proximally inside the tibia. Venable and Stuck [6] state, "No screw holds well in cancellous bone." To engage the opposite cortex of the tibia would require a rather long screw (fig. 2, *C* and *D*).

2. The metal does not enter the fracture site itself but surrounds it from the outside. This preserves all cancellous bone for contact with the intramedullary bone graft. A screw inserted into the malleolus replaces some cancellous bone material, and its position must be checked by roentgenograms to rule out possible encroachment of the joint itself. Once a screw has been introduced, any further adjustment which may be required will endanger the rigid fixation which is so desirable.

3. There is minimal damage to the remaining blood supply of the malleolar fragment by avoiding the insertion of a screw through the tip of the malleolus. This is the point of attachment of the ligamentous structures which contain important vascular elements.

4. In contrast to screw fixation, the hookplate is effective in the presence of osteoporotic bone and does not split the fragment.

5. Because of the solid type of fixation, prolonged plaster fixation is not required, and early mobilization without weight bearing can be encouraged.

6. The hookplate, which is commercially available in different sizes, can be bent easily to conform to the contour of the bony structures and is well tolerated by the overlying skin.

7. I have not observed structural weakness of the commercially available hookplates if they are properly introduced after a hairline reduction has been obtained. It should be stressed again that the hooks have to be introduced into prepared holes; otherwise, they frequently will straighten out and not engage directly the small fragment. This experience contrasts with that in one report which indicates structural weakness with loss of the desired solid fixation allowing renewed displacement. Still, this criticism has to be taken seriously, and every effort should be made to standardize the quality of the material by the manufacturing companies.

Comment

Many different gadgets have been described for fixation of fractures of the shaft of the long bones and of the neck of the femur (screws, plates, slotted plates, bands, wires, and intramedullary nails). Very few, however, have been developed for fixation of a small bone fragment which is either important for structural joint stability or is essential for ligamentous attachment. One might, therefore, conclude that none is needed. Wire or screw fixation may give satisfactory results, but there are a number of conditions which cannot be treated adequately by these conventional methods. It is felt that the hookplate fills a definite need and enables the surgeon to deal successfully with this group of fractures for which there is no satisfactory method of internal fixation. Nonunion of the medial tibial malleolus may be classified in this latter group. Ten such cases have been treated successfully with the hookplate, and bony union resulted in all of them within 10 weeks. The functional results, of course, do not depend entirely upon the bony union of the medial malleolus, but this aspect of the injury was dealt with successfully in every case.

In evaluating the technical aspect of this method of fixation, it should be stated that this report on the hookplate is not based on these 10 cases alone but on over 350 other cases in which patients have been treated during the past 10 years in a similar way.[7] This method has given consistently reliable fixation of small bone fragments with an extremely high rate of bone union. No displacement of the fragment has been observed such as is occasionally seen with other types of fixation. The hookplate has been applied for (1) fresh or recent fractures of the medial or lateral malleolus, (2) comminuted fractures of the medial malleolus, (3) malunited medial malleolar fractures, (4) comminuted olecranon fractures, (5) fixation of small fragments of other joints (knee, shoulder, and hip), and (6) fractures of the distal tibial epiphysis.

The objection to the hookplate which has been raised by Riess,[8] Buck-Gramcko,[9] and Fackert [10] is based on the requirement for broader exposure and more extensive surgery than with some other methods. This seems unjustified, since in none of my 350 cases was there any breakdown of the surgical wound or the overlying skin. In order to accommodate the hookplate, the incision must be extended proximally 1 or 2 cm. more than is required for simple screw fixation. No harmful effect of any kind has been observed from this added length. It should also be noted that the introduction of a screw in a very oblique direction to avoid encroachment on the joint requires a longer distal incision than is customary with the use of the hookplate. In all cases the hookplate has enabled me to deal successfully with the fixation of small fragments, regardless of their size, shape, or bony consistency.

Summary

The hookplate has been used as a method of treatment for nonunion of the medial tibial malleolus. Ten fractures have been treated, with excellent anatomic and functional results. This method has certain advantages over other forms of internal fixation.

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RETROSTERNAL PLACEMENT OF ASCENDING COLON FOR ESOPHAGEAL SUBSTITUTION

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and
Jose H. Amadeo, M.D., Philadelphia

Reestablishment of continuity of the passage from pharynx to stomach after removal of a diseased esophagus, or in the absence of the esophagus, formerly depended on the use of external tubes constructed of skin, stomach, or small intestine. These have been unsatisfactory for various reasons. Since 1951 it has been possible to reestablish the connection of pharynx to stomach by a retrosternal segment of colon within the thorax. Three cases are described illustrating the usefulness of this procedure in three types of esophageal disease. In one patient, a 64-year-old man, carcinoma had infiltrated most of the esophagus, and a previously unsuspected fungating carcinoma was found in the stomach at operation. The substitution of a segment of colon for the esophagus was successfully carried out, and the transplanted colon functioned well for six months until death. Substitution of colon for esophagus likewise succeeded in an 11-year-old girl with esophageal stricture after the ingestion of lye, and in a 3-year-old boy born with complete atresia of the esophagus. In both children subsequent growth has been normal. This type of operation is recommended particularly for benign lesions of the esophagus in which long-term survival is anticipated.

The surgical management of congenital and acquired lesions of the esophagus presents unusual problems not common in other forms of surgical therapy. Nearly half a century has elapsed since Torek [1] reported the first successful resection of the thoracic esophagus. External tubes were used to replace the esophagus. Many methods used since that time for the reestablishment of continuity after partial or complete resection of this organ have not proved entirely satisfactory. This is particularly true after esophageal resection for benign lesions, after which long-term survival is anticipated. Recent experiences in which an isolated segment of colon is used to replace the esophagus suggest that this method may be preferable in many instances to those heretofore employed.

The employment of segments of colon for esophageal substitution is not new. A successful case was reported by Kelling [2] as early as 1911 and the advantages of using part of the colon as a subcutaneous esophagus were discussed by Vulliet [3] in the same year. Von Hacker [4] reported the successful use of this method in 1914. Orsoni and Toupet [5] described the first case in which a segment of colon was carried as high as the neck through a subcutaneous tunnel in 1930. Scattered reports of similar procedures have appeared in the European literature.

Replacement of the esophagus by a part of the colon within the thorax was first described by Rudler [6] in 1951. He placed a segment of ascending colon and ileum retrosternally as a palliative procedure in a patient with carcinoma of the esophagus. Lortat-Jacob [7] used a segment of ascending and transverse colon in the same year for a case of lye stricture of the esophagus. The distal end of the colon segment was anastomosed to the jejunum in both instances. In 1952, Robertson, Howe and Smithwick [8] reported a successful case of esophageal substitution in which the transverse colon was interposed between the esophagus and jejunum. Kergin,[9] in 1953, employed a staged procedure in the insertion of a segment of transverse colon to bypass a high esophageal obstruction due to mediastinal paraffinoma. Battersby [10] reported an experimental and clinical study in 1953. Additional patients with carcinoma of the esophagus so treated were reported by Mahoney and Sherman [11] in 1954. Dale [12] and Sherman [13] utilized segments of ascending colon in three patients with esophageal atresia and in two additional patients with carcinoma of the esophagus in 1955.

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Replacement of the esophagus by segments of colon, especially for benign lesions, may prove superior to other procedures for several reasons. The colon is more resistant to acid gastric secretion than the jejunum or the esophagus itself.[14] Reestablishment of esophageal continuity can therefore be accomplished without the need to bypass the stomach. A sufficient length of viable colon is easily mobilized for even the highest anastomosis in the neck. The adequacy of the blood supply may be determined prior to mobilization of the colon by the observation of the colon during application of vascular clamps to the vessels requiring ligation. In some cases, sufficient length is obtained so that the cecum, the ileal stump, and the appendix can be safely removed, thus eliminating two of the suture lines. This was possible in two of our patients. Adequate preoperative preparation with neomycin and other agents is probably helpful.

It seems worthwhile to report our experience with three consecutive patients in whom isolated segments of colon were used to replace the esophagus. These three patients, one of whom had carcinoma of the esophagus, one congenital absence of the esophagus, and one lye stricture of the esophagus, illustrate the variety of esophageal lesions that may be treated by this method.

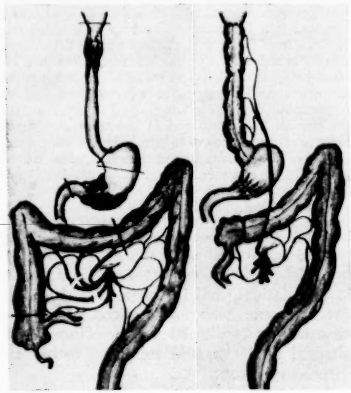

Fig. 1 (case 1).—Lesions, vascular pattern, and reconstruction.

Report of Cases

Case 1.—A 64-year-old man was admitted to Jefferson Medical College Hospital on March 23, 1956, with a history of progressive dysphagia for six months. He had lost 35 lb. (15.9 kg.). Barium swallow revealed the esophagus to be almost completely obstructed by an infiltrating lesion beginning 3 cm. below the larynx.

Operation was performed on March 30, 1956. A cervical and an anterior thoracotomy incision, both on the right side, were used to mobilize the proximal and thoracic portions of the esophagus. The abdomen was then opened through a midline incision, and a previously unsuspected fungating carcinoma of the stomach was found. A radical subtotal gastric resection was carried out and a Billroth 1 type of anastomosis performed. The ascending and transverse colon were then mobilized. Three middle colic arterial branches were present. It was necessary to divide the right colic artery and two right-middle colic arterial rays. The colon was divided just distal to the cecum and again just distal to the midtransverse colon. The single remaining middle colic artery provided an adequate blood supply for the entire colonic segment, which was brought up to the neck through a retrosternal tunnel and anastomosed to the pharynx and the gastric fundus. Colonic continuity was reestablished by a colocolostomy. In this case the total esophagectomy and radical subtotal gastrectomy were well tolerated by the patient. The postoperative course was uneventful except for a single episode of atelectasis of the right lung, which was treated by two bronchoscopic aspirations. The patient was discharged on the 15th postoperative day able to eat a full diet. The histological diagnoses were (1) poorly differentiated squamous cell carcinoma of the esophagus and (2) adenocarcinoma of the stomach, intermediate grade.

The patient died in September, 1956, six months after operation, in another hospital. Postmortem examination revealed cerebral metastasis, but it is not known whether this was secondary to the esophageal or to the gastric carcinoma. The patient had clinical evidence of other distant metastases. He obtained excellent palliation, and the transplanted colon functioned well until his death.

Comment.—It was fortunate that the colon was prepared with antibiotics in this case. Had the colon not been so prepared, it is unlikely that continuity could have been easily reestablished by other means after a radical subtotal gastric resection. Anatomic variation in the midcolic artery in this patient is shown in figure 1. In cases of esophageal carcinoma in which the lesion cannot be removed, bypass alone can provide palliation.

Case 2.—A boy was born on March 2, 1953, with complete atresia of the esophagus. Twenty-four hours after birth a pharyngeal fistula was established on the left and a gastrostomy performed in another hospital. The child was fed through the gastrostomy and at the same time encouraged to swallow foods in order to establish the swallowing reflex.

On Nov. 5, 1956, the patient was admitted to Jefferson Medical College Hospital for consideration of esophageal reconstruction. Roentgenographic examination revealed no distal esophageal segment. On Nov. 16, 1956, the patient was operated on under general anesthesia. The ascending colon was mobilized through a midline abdominal incision. Two midcolic arterial branches were found. The right midcolic branch and the ileocolic arteries were divided. The terminal ileum was divided and its distal stump inverted. The transverse colon was divided just to the left of the midcolic artery. An ileotransverse colostomy was then carried out. The pharyngeal fistula was mobilized through a left transverse cervical incision. The pharynx was extremely thin and attenuated. A tunnel was made in the retrosternal space and the colon was rotated so that the appendix, cecum, and terminal ileum were delivered through the lateral cervical incision. Because of the length of colon obtained it was possible to amputate the colon distal to the cecum and remove the cecum, terminal ileal stump, and appendix. The colon was then anastomosed to the pharynx and stomach and the wounds closed (fig. 2).

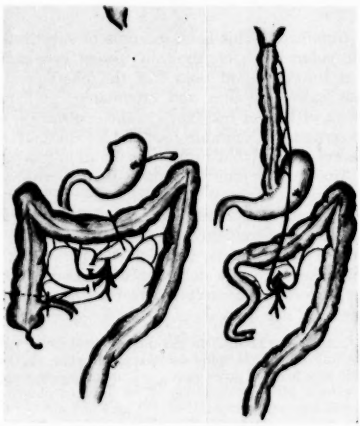

Fig. 2 (case 2).—Vascular pattern and reconstruction.

The postoperative course was uneventful, and the patient was discharged two weeks after the operation. The x-rays are shown in figure 3. The patient was eating a full diet on the eighth postoperative day, and the gastrostomy tube remained clamped until its removal two months later. The patient was seen on Sept. 26, 1957, and remains asymptomatic. There is no difficulty in swallowing, and he can eat a full diet. His growth and nutrition are normal.

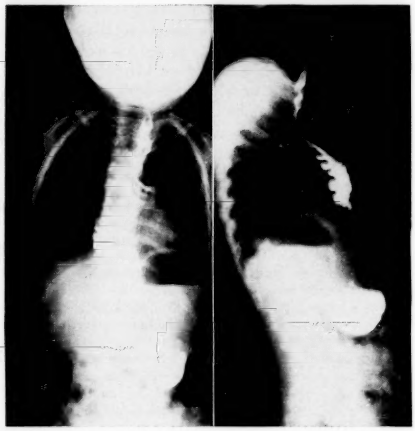

Fig. 3 (case 2).—*Left*, anteroposterior and, *right*, lateral postoperative barium swallow x-rays.

Comment.—This is an example of substitution of the colon for a congenitally absent esophagus. It was interesting to note that the pharyngeal wall was extremely thin and attenuated, perhaps the result of lack of resistance to the contraction of the pharyngeal musculature. A different anatomic variation of the midcolic artery was found in this patient.

The gastrocolonic anastomosis was performed on the lesser curvature of the stomach with the consideration that should peptic colitis develop a proximal gastrectomy could be performed more easily. Resection of the vagi was not required in this case, so that a decompression gastroenterostomy, pyloroplasty, or pyloromyotomy was not necessary.

Case 3.—An 11-year-old girl was admitted to the Jefferson Medical College Hospital for the fourth time on Oct. 23, 1956. She had had an extensive stricture of the entire thoracic esophagus after the ingestion of lye six years previously. A gastrostomy was performed at that time and she was treated with periodic esophageal dilatations for three years. She was then readmitted because of pneumonitis and failure of dilatation to provide an adequate esophageal lumen. A thoracotomy was performed on the left and esophageal dilatation carried out under direct vision. This operation was complicated by postoperative staphylococcic abscesses in the left lung and empyema on the left. The child recovered slowly, and an adequate nutritional status could be maintained by esophageal bougienage and gastrostomy feeding. Despite repeated esophageal dilatations she again developed dysphagia and was readmitted for consideration of esophageal bypass. On Nov. 19, 1956, the patient was again operated on. The proximal esophagus was exposed and mobilized through a right oblique cervical incision. It was divided and the distal segment closed. The abdomen was opened through a paramedian incision on the right, and the ascending and transverse colon mobilized as previously described. A single midcolic artery was present. The distal ileum was divided and its stump inverted into the cecum. The transverse colon was divided to the left of the midcolic artery and an ileotransverse colostomy carried out. The cecum and ascending colon were brought up to the cervical incision through a tunnel behind the sternum. The appendix was removed and the greatly hypertrophied proximal esophageal segment anastomosed to the cecum. The distal end of the transplanted colonic segment was anastomosed to the stomach (fig. 4). Her postoperative course was uneventful, and when discharged she was eating a full diet without difficulty. On Dec. 13, 1956, the gastrostomy was closed, and she has since remained completely asymptomatic.

Comment.—This case presents an example of colonic substitution of the esophagus for an acquired benign lesion. Vagotomy was not necessary in this patient, and therefore a gastric decompression operation was not required. She has obtained an excellent result after years of unsuccessful esophageal dilatation and continues to eat a full diet without symptoms.

A third variation of the midcolic artery was present. The extreme hypertrophy of the proximal esophageal segment in this patient was interesting. It was probably the result of swallowing against the resistance provided by the esophageal stricture.

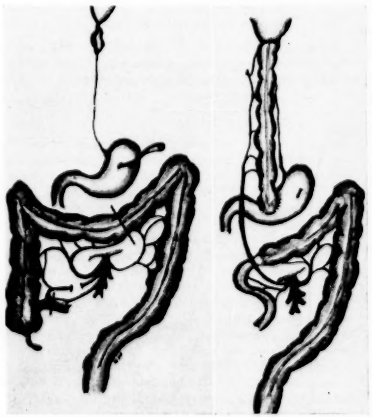

Fig. 4 (case 3).—Vascular pattern and reconstruction.

Summary

Three successful consecutive esophageal substitutions by retrosternal transplantation of the colon were performed, one for carcinoma of the esophagus, one for congenital absence of the esoph-

agus, and one for acquired stricture of the esophagus. In each instance the patient obtained an excellent functional result from the operative procedure employed, and no serious difficulties were encountered in the postoperative period.

No evidence of peptic colitis was noted during the follow-up period of 6 months in one and 11 months in two patients. We suggest that isolated colonic segments be utilized for esophageal substitution more frequently. This technique is recommended particularly for benign lesions of the esophagus in which long-term survival is anticipated.

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USE OF ARTIFICIAL KIDNEY.—The terminal stage of acute uremia, characterized by coma, convulsions or severe cardiac failure, is not the best possible time for dialysis, even though some patients can yet be saved at this late stage of the artificial kidney. . . . It is not often realized . . . that (*a*) terminal stages are often not reversible with or without dialysis, (*b*) preterminal stages frequently deteriorate within a matter of hours into terminal stages, and (*c*) irreversible (or slowly reversible) injury to nervous or circulatory systems can occur early (before the 10th day) in the course of acute anuria. It has been proposed that a skilled and experienced physician is able to postpone dialysis or avoid it entirely. One should receive this argument with the utmost skepticism, inasmuch as it is unsupported by evidence. . . .

I . . . favor initial hemodialysis (*a*) whenever necessary for electrolyte abnormality; (*b*) if there are any clinical signs, on the fifth day of anuria-oliguria; (*c*) if there are no clinical signs but continuing oliguria on the sixth day; (*d*) thereafter, repeat dialysis whenever indicated clinically or by serum electrolytes or by BUN over 150. If we had adopted a rule to dialyze all patients who remain anuric for five or six days, we would have dialyzed an additional six patients who recovered without the use of the artificial kidney and where this treatment would have been superfluous. We would also have dialyzed 16 of the 17 patients in whom the artificial kidney was applied too late, with an unknown and unknowable, but probably very considerable, salvage. In view of the very small risk, the conclusion is inescapable that early use of the artificial kidney would have been preferable in the present series of patients.—P. F. Salisbury, M.D., Ph.D., Timely Versus Delayed Use of the Artificial Kidney, *A. M. A. Archives of Internal Medicine,* April, 1958.

POSTHEMIPLEGIC REFLEX SYMPATHETIC DYSTROPHY

Eugene Moskowitz, M.D., Harold F. Bishop, M.D., Hla Pe, M.B., B.S.
and
Kinichi Shibutani, M.D., Valhalla, N. Y.

Hemiplegia in the six cases here described was followed by a painful syndrome in the affected upper extremity. Progressive changes were observed in soft tissues, joints, and bones. Ipsilateral stellate ganglion blocks afforded prompt but not always permanent relief, and the two patients who submitted to high thoracic sympathectomy obtained lasting benefit. The evidence showed that much of the disability represented inhibition caused by severe pain and trophic changes. The prompt remission of the symptoms after sympathetic block or sympathectomy enabled the patient to utilize powers still latent in the extremity and greatly facilitated the program of rehabilitation.

Multiple complaints referable to the extremities are frequently encountered during the rehabilitation of patients with cerebral lesions, particularly cerebral vascular accidents. These symptoms may often prevent the successful completion of a rehabilitation program. Many of these patients have a relaxation of the shoulder capsule associated with pain, due to traction of the paralytic extremity. In these patients, Tobis [1] has recently recommended the use of a sling, with proper positioning of the arm at night to restore the normal anatomic alignment of the shoulder joint.

Occasionally, one may encounter multiple peripheral manifestations in the paralytic upper extremity without any relaxation of the shoulder joint. These patients present the symptom complex referred to as the shoulder-hand syndrome. Chevallier [2] in 1867 called attention to vasomotor disturbances in hemiplegic patients. Later, Sudeck [3] described post-traumatic atrophy of the hand after injury. Miller and de Takats [4] referred to it as a post-traumatic dystrophy. Evans [5] summarized 57 cases of reflex sympathetic dystrophy occurring in a number of disabilities, including a hemiplegic patient. Steinbrocker [6] clearly defined the total picture of the shoulder-hand syndrome in reflex dystrophy of the upper extremity. He included a hemiplegic patient in his series. Repeated sympathetic blocks were recommended by several authors for the treatment of this syndrome. Swan [7] described the shoulder-hand syndrome in three cases after hemiplegia. Betcher and Casten [8] outlined the criteria for the treatment of various stages of the disability as classified originally by Steinbrocker. Most recently, Rosen and Graham [9] reviewed 73 patients with shoulder-hand syndrome. They called attention to the need for early recognition of this disability. There were several patients with cerebral lesions included in their series. In the past three years, we encountered six cases of reflex sympathetic dystrophy of the upper extremity during the rehabilitation of a large number of patients with cerebral vascular lesions.

Report of Cases

Case 1.—A 67-year-old male had a cerebral thrombosis with hemiplegia on the right side and moderate degree of expressive aphasia. Five months later, he complained of severe pain in the right upper extremity involving the shoulder, elbow, and the fingers. The hand and the fingers were swollen, the skin was red and warm, and there was marked limitation of passive motion in the fingers. Conservative treatment including heat, massage, and passive exercises gave no relief. After a right stellate ganglion block, there was immediate alleviation of the pain in the hand and fingers. The swelling subsided and there was some return of voluntary function. Active exercises were instituted without pain. However, pain and limitation of motion in the shoulder persisted. The shoulder pain was relieved by a right suprascapular nerve block but motion was unchanged. The elbow was completely stiff due to the development of an extensive heterotrophic calcification (fig. 1).

Case 2.—A 60-year-old male had a cerebral thrombosis which resulted in hemiparesis on the right side with expressive aphasia. He improved to the extent that he was ambulant and able to use his right hand. One year later, he developed progressive pain in the right shoulder. The hand and fingers became stiff and swollen with increased skin temperature, and there was progressive loss in shoulder motion. All attempts at motion were strongly resisted by the patient who became rather emotionally unstable. Right stellate ganglion blocks were performed on three occasions during one week. There was definite relief of pain and increase in finger and hand motion after each block, but the shoulder was unaffected. Despite vigorous physical therapy, the symptoms in the hand recurred. High thoracic sympathectomy on the right at the level of T-2 and T-3 was performed, with prompt improvement in the symptoms. After vigorous treatment he regained a considerable degree of painless function in the hand and fingers but the shoulder remained partially frozen (fig. 2).

Case 3.—A 42-year-old female developed hemiplegia on the left side after craniotomy for excision of a meningioma. She had some function in the lower extremity, but the arm was flaccid with painless, passive complete motion. During the course of her physical rehabilitation she developed a burning pain in the left hand and fingers associated with swelling, obliteration of the interphalangeal joint creases,

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stiffness, and trophic changes in the skin. Passive motion of the hand and fingers became progressively intolerable and the patient became emotionally unstable. A left stellate ganglion block was performed with temporary amelioration of the symptoms. However, the pain recurred with increased intensity. A second stellate ganglion block was done with

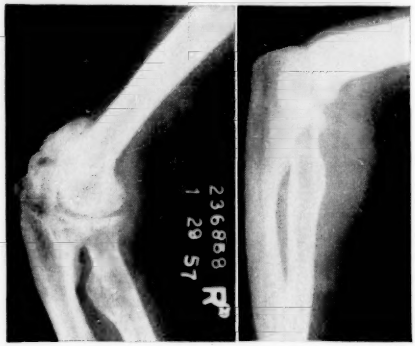

Fig. 1.—Extensive periarticular calcification of elbow in hemiplegic patient *(left)* compared with other elbow *(right)*.

gradual relief of pain, permitting the resumption of physical therapy. Voluntary power returned gradually over a period of several months. Seven months after discharge, there was about 90% restoration of function in the entire upper extremity without any contractures.

Case 4.—A 70-year-old female developed hemiplegia on the left side after a cerebral thrombosis. Two months after the onset of the hemiplegia, she complained of pain in the left hand and fingers. The hand was warm, red, slightly swollen, but without pitting edema. The skin was rather smooth and glistening. All attempts at passive motion were resisted with progressive limitation of motion, particularly in the proximal interphalangeal joints. She had fairly good function in the thumb. There was prompt relief of pain after a left stellate ganglion block was done, with increased range of motion. The pain recurred within several hours with increased severity. Two subsequent blocks, with lidocaine (Xylocaine) hydrochloride, afforded temporary relief. High thoracic sympathectomy on the left at T-2 and T-3 was performed. The pain and swelling subsided gradually with some return of joint motion, permitting the resumption of active physical therapy. The interphalangeal creases reappeared. However, the contractures in the proximal interphalangeal joints remained despite the return of power in the fingers. This patient is now able to grasp and utilize the hand in an assistive capacity. Motion in the shoulder is still restricted.

Case 5.—A 48-year-old female had a cerebral thrombosis with hemiplegia on the left side. She was taught to walk with a short leg brace, but there was no return of power in the left upper extremity. Passive motion in the left shoulder became increasingly painful and restricted. Several weeks later, it was noted that the hand was discolored, slightly swollen, moist, and clammy. The fingers were flexed at the proximal interphalangeal joints but the thumb was held in extension. There was a marked degree of emotional instability. Physical therapy afforded no relief. Repeated left stellate ganglion blocks provided prompt but temporary relief. Unfortunately, this patient has refused definitive surgery.

Case 6.—A 59-year-old male with a history of coronary thrombosis had a cerebral vascular accident with hemiplegia on the left side. After two months, he complained of pain in the left shoulder, especially during the night. Subsequently, his wrist and fingers became quite painful and somewhat swollen, with marked limitation of passive motion. He had no active joint function. Two weeks of conservative therapy consisting of locally applied heat and gentle passive exercises did not relieve the symptoms. A left stellate ganglion block was performed and this brought considerable relief. Rehabilitative activities were resumed. At the present writing, there has been no return of active function in the hand, but there is practically a full range of painless passive motion with no swelling or trophic changes noted.

Comment

Although the incidence of reflex sympathetic dystrophy in hemiplegic patients is rather infrequent, early recognition and treatment is desirable in order to prevent the irreversible effects of the disability. It would be presumptuous to assume that either the sympathetic block or the sympathectomy was responsible directly for the return of active function in the hands of four of these six patients. It is more reasonable to assume that the function was inhibited by the severe pain and trophic changes, and the prompt remission of the symptoms enabled the patients to utilize the latent power in the hand.

The symptoms as presented in the six cases described have been amply discussed by previous authors, particularly Steinbrocker, and present no unusual manifestations. However, it might be interesting to note that the diagnosis of acute rheumatoid arthritis was made in case 5. All of these patients presented emotional problems such as depression and instability. The aphasic patients were presumed to have an organic brain syndrome. Observation of these cases during the course of the

Fig. 2.—Extensive osteoporosis of frozen shoulder in hemiplegic patient.

disability would seem to indicate that these emotional symptoms followed rather than preceded the physical manifestations in the extremity.

Frequently one encounters swelling, pitting edema, and cyanosis of the hand in hemiplegic patients. This is usually due to stasis or possibly to an

unrecognized thrombophlebitis. Prompt positioning of the extremity with adequate physical therapy usually relieves this condition. In patients presenting the syndrome of reflex sympathetic dystrophy, the swelling is usually less pronounced, without pitting edema but with rather marked trophic changes in the skin. The proximal interphalangeal joints are primarily involved. X-ray examination during the later stages reveals the typical changes in the carpal bones, as originally described by Sudeck, consisting of spotty demineralization which persists even after the patient has improved. Figure 3 illustrates the hands of the patient in case 1, and figure 4, by contrast, shows the x-rays of the hands of a hemiplegic patient without any dystrophic changes.

Early recognition of the disability is important since the contractures in the fingers may become irreversible in a relatively short time. Prompt blocking of the stellate ganglion with short-acting anesthetics, such as procaine or lidocaine, can be utilized as a diagnostic–therapeutic procedure. In some cases it was noted that the symptoms recurred with increased severity after the temporary relief afforded by the first stellate ganglion block. In case 4, considerable persuasion was necessary to get the patient to consent to an additional blocking procedure. Sympathectomy was performed only after repeated blocks had failed to produce a lasting remission. Symptoms referable to the shoulder, including pain and limitation of motion, were not favorably affected by either the blocks or the sympathectomy.

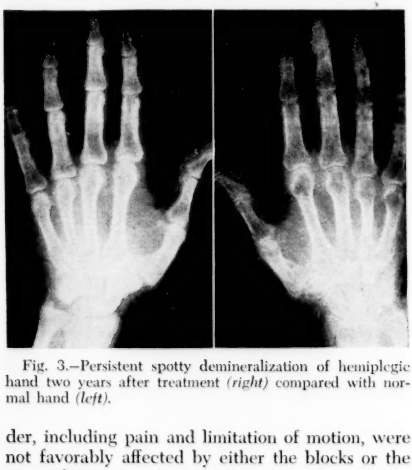

Fig. 3.—Persistent spotty demineralization of hemiplegic hand two years after treatment *(right)* compared with normal hand *(left)*.

Summary

As observed in six cases of posthemiplegic reflex sympathetic dystrophy of the upper extremity, early recognition of this unusual complication is necessary to prevent irreversible contractures and disability. Ipsilateral stellate ganglion blocks are an important diagnostic-therapeutic procedure in the early stages of this disability if they are followed by adequate mobilization. If repeated blocks have given temporary relief, high thoracic sympathectomy is the definitive treatment of choice. The underlying shoulder disability is unaffected by the blocks or sympathectomy.

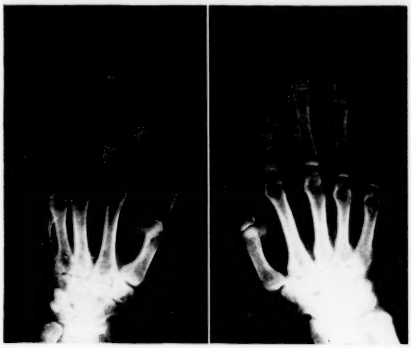

Fig. 4.—Hemiplegic hand without dystrophic changes *(left)* and uninvolved hand of same patient *(right)*.

Addendum

Since the completion of this report, two additional patients have responded favorably to stellate ganglion blocks and vigorous physical therapy.

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CLINICAL NOTES

INTRA-ARTICULAR ADMINISTRATION OF HYDROCORTISONE IN HIGH CONCENTRATION

USE IN TREATMENT OF ARTHRITIC KNEES

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The value of hydrocortisone given intra-articularly in the treatment of arthritis has been well established by a number of investigators. In addition to hydrocortisone acetate, various analogues and derivatives of hydrocortisone have been studied. As a result of these studies, certain specific dose recommendations have been made.

Hollander and associates [1] have studied extensively this means of therapy and in one study based on 1,700 injections [1c] suggested that the way is open to finding analogues or esters of hydrocortisone having still more lasting palliative effect. Hollander has recommended injections of from 25 to 50 mg. of hydrocortisone acetate, with 50 mg. as the maximum dose.[1d] This upper-dose recommendation was based on the apparent inability of the synovial lining of the joint to absorb efficiently a greater quantity of the drug because of the "overflow effect" leading to systemic manifestations. In my experience, however, doses of this magnitude have not achieved optimum results. Improvement has been inadequate and too transient to be completely satisfactory either to the physician or to the patient.

The Present Study

The purpose of this study was twofold. First, I was interested in a comparative evaluation of the effects of various compounds of hydrocortisone when injected into the joint cavity. My second interest concerned the effect of comparatively high doses of hydrocortisone acetate by this route. In pursuit of my first objective, I evaluated hydrocortisone acetate and hydrocortisone tertiary-butylacetate. More recently I have studied the acetate of Δ^1-hydrocortisone (prednisolone acetate).

Several investigators [2] have reported the increased duration of symptomatic relief obtained after the use of hydrocortisone tertiary-butylacetate in a large proportion of patients. In a minority of patients, a greater degree of symptomatic relief was achieved than with equivalent doses of hydrocortisone acetate. However, not all patients have responded to the tertiary-butylacetate, and a significant number have been noted to achieve greater relief of symptoms and signs from the acetate than from the tertiary-butylacetate. In general, my experience with hydrocortisone tertiary-butylacetate has paralleled that of other investigators. I found it to be somewhat more effective than the acetate and to approximately double the average duration of symptomatic relief over that of hydrocortisone acetate in the majority of patients. In others, however, it proved to be inadequate.

Because of the inadequate response in some patients to doses of the order of 25 to 50 mg., I proceeded to increase the dose of hydrocortisone acetate far beyond this usual dose. It was my feeling that in large joints the greater area of synovial tissue should permit a greater absorption of hydrocortisone. The preparations used in this study were furnished in concentrations of 50, 100, 150, and 250 mg. per milliliter. Some contained neomycin, 5 mg. per milliliter, as an antibacterial agent.

TABLE 1.—*Response of Sixty Patients with Arthritis to Various Steroid Preparations**

	Patients		Improvement					
				Duration, Days				
	No. Injected	No. Improved	Grade†	Min.	Av.	Max.	Injections, Total No.	Patients with Systemic Effects, No.
Hydrocortisone acetate, 25-50 mg.	60	45§	2-3	3	6	14	202	5
Hydrocortisone tertiary-butylacetate, 25-50 mg.	60	51	2-3	3	11	30	186	2
Hydrocortisone acetate, 150-300 mg.‡	60	36‖	1-2	21	34	80	303	<40¶
Hydrocortisone acetate, 250 mg./cc.	40	38	1-2	20	31	76	235	36
Prednisolone acetate, 25-50 mg.	50	40	2-3	5	10	25	95	7

* Eleven patients had osteoarthritis and 49 had rheumatoid arthritis.
† Grade 4, little or no relief; grade 3, moderate relief; grade 2, marked relief; grade 1, complete relief.
‡ Some preparations contained neomycin, 5 mg. per milliliter.
§ Of the patients whose condition did not improve, six had osteoarthritis and nine had rheumatoid arthritis.
‖ Of the patients whose condition did not improve with large doses, three had osteoarthritis and one had rheumatoid arthritis. The two patients whose condition did not improve after therapy with 250 mg. per cubic centimeter of hydrocortisone acetate also showed no improvement after therapy with 150 to 300 mg. of hydrocortisone acetate (column 3).
¶ Systemic effect was not evaluated in every patient.

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Sixty patients were studied with reference to the degree and duration of response to different preparations and to varying doses. The knee joint was used throughout the study. The group consisted of 11 patients with osteoarthritis and 49 patients with rheumatoid arthritis. The patients shown in the first column of table 1 received hydrocortisone acetate in the usually administered dose of 25 to

TABLE 2.—*Systemic Effects in Patient with Rheumatoid Arthritis, Stage 2, Class 3*

Date, 1955	Knee Injection (Hydrocortisone Acetate), Mg.	Eosinophil Count, No./Cu. Mm.	Steroid Excretion, Mg./24 Hr.	
			Free, Porter-Silber*	Free, Gornall-McDonald†
2/19		568		
2/20		481	0.588	
2/22			0.594	
2/23		380	0.478	1.025
2/24	250‡	258 (8 a.m.)	0.745	1.59
2/25		120	1.148	2.96
2/26		0	1.739	3.08
2/27		6	1.423	2.65
2/28		0	1.358	
3/1		109	1.190	1.91
3/2		246	0.640	1.01
3/3				1.44
3/4	250‡	371 (8 a.m.) 212 (at 6 hr.) 160 (at 24 hr.)		1.41
3/5		25		2.77
3/7		40		6.84
3/8		34		4.20
3/9		80		2.70
3/10		69		1.79
3/11		200		
3/12		181		
3/13		250		
3/14		206		
3/15		212		
3/16		230		1.015
3/17		258		
3/18		303		
3/21		260	0.445	1.60
3/22				
3/23	250‡	287 (8 a.m.) 200 (at 5 hr.) 110 (at 18 hr.)	0.334 1.115 1.605	
3/24				5.77
3/25		48	1.710	8.00
3/28		60	1.402	5.65
3/29		24	1.113	3.80
3/30		68	0.896	3.77
3/31		180		
4/1		203	0.468	1.98
4/2		281		1.55
4/4		290	0.523	1.13
4/5		275		
4/6		304		

* Porter and Silber: J. Biol. Chem. **185**:201, 1950. Kassenar and others: Acta endocrinol. **18**:99, 1955.
† Gornall and McDonald: J. Biol. Chem. **201**:279, 1953.
‡ Intra-articular, at 8:30 a.m.

50 mg. Next, in column 2, are the results of tests with the higher ester, hydrocortisone tertiary-butylacetate, with the dose still held at the 25-to-50-mg. level. In the third column are recorded the results with the large doses (150-300 mg.) of hydrocortisone acetate with neomycin. Hydrocortisone acetate, 250 mg. per milliliter, was employed in the 40 patients shown in column 4. Prednisolone acetate, 25-50 mg., produced the results depicted in the last column.

I was particularly impressed by the results obtained with the higher dose range (150-300 mg.) of hydrocortisone acetate. Significantly, both the number of patients who obtained relief and the degree of relief obtained were greater than was observed with the same preparation in 25-to-50-mg. doses. Of equal or perhaps greater importance, the duration of improvement rose from an average of 6 days to an average of 34 days.

It is interesting to note that in column 3 there are 56 patients with conditions improved (93.3%) as compared with 45 patients (75%) in column 1. The degree of improvement, however, points up the real significance of the results. Along with an 18.3% increase in the number of patients with their condition improved by larger dosage, the marked improvement from grade 3 in column 1 to grade 1-2 in column 3 is striking.

It has been noted by other investigators [3] that hydrocortisone is systemically absorbed from the joint cavity. Clinical manifestations of this absorption were reported by Ward and Mason,[3b] who noted that in 21% of their patients a generalized antirheumatic effect followed intra-articular injection of hydrocortisone acetate. Ninety per cent of those patients in whom a systemic effect was observed received intra-articular injections of 50 mg. or more. In this group, improvement in uninjected joints was observed to follow the intra-articular injection of hydrocortisone in a single joint. Coincident with the quantitative and qualitative improvement observed with the larger dose of hydrocortisone acetate in our series was an increase in the incidence of systemic manifestations. These rose from 5 (column 1) to over 40 (column 3). Subjective improvement in other affected but uninjected joints was the clinical manifestation noted. A reduction in total eosinophil count and an increase in the amount of 17-hydroxycorticosteroids in the urine was also noted. Table 2 contains data on eosinophil count and steroid excretion that are illustrative of the systemic effect produced. The occurrence of systemic effects was coincidental and not intentional. However, these effects caused no difficulty and, in fact, seemed to evoke gratitude from many patients. There were no "flare ups" after systemic relief disappeared. The neomycin included in some of the preparations produced no evidence of reaction in the joints and no evidence of systemic toxicity. Urine examination revealed no change after the administration of neomycin.

Summary and Conclusions

Larger doses of hydrocortisone acetate than heretofore generally employed may be injected into the larger joints such as the knee joint, with quantitative and qualitative improvement in results over those obtained with smaller doses. Quantities of

hydrocortisone acetate suspension as great as 5 to 6 cc. were given without reaction either to the volume or to the amount of hydrocortisone.

No toxic or other untoward effects were noted with the injection of neomycin in amounts up to 25 to 30 mg. into the joint. The addition of neomycin affords effective antibacterial protection against possible septic infection of the joint. Systemic effects manifested by improvement of uninjected joints, lowered eosinophil counts, and increased urinary steroid values occurred with larger doses of hydrocortisone acetate.

These findings suggest that the larger joints, such as the knee, have a greater capacity than heretofore believed to hold a larger quantity of hydrocortisone in the cells. Thus a greater and more intense degree of improvement as well as an increased duration of relief will follow.

Addendum

Since this paper was prepared for publication, similar clinical and laboratory results have been reported in five patients by Fujita.[4]

40 North St. (2).

The hydrocortisone tertiary-butylacetate, 25 mg. per ml., used in this study, was supplied by Merck, Sharp & Dohme, Rahway, N. J. The prednisolone acetate, hydrocortisone acetate (50 mg. per milliliter with neomycin, 5 mg. per milliliter), and other hydrocortisone acetate preparations in concentrations of 50 mg. to 250 mg. per milliliter were supplied by the Upjohn Company, Kalamazoo, Mich.

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CHERNEY INCISION IN UROLOGIC SURGERY

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Edward Bigg, M.D., Chicago

The urologist has occasion to utilize surgical procedures which necessitate an easy access to the deepest pelvic recesses. An adequate incision will facilitate these deep pelvic operations and result in reduced surgical trauma to the patient and lessened strain on the surgeon. The Cherney incision, with division of the tendinous insertions of the rectus muscles at the symphysis and with lateral extension, gives pelvic access superior to that of any previously described incision.

Pfannenstiel, in 1900, suggested transverse division of the lower abdominal skin and fascia with separation of the rectus muscles. In 1907, Maylard and Bardenheuer modified the Pfannenstiel incision by dividing all the lower abdominal layers transversely. Maylard, in a paper supplemented by excellent drawings, discussed the transverse incision for abdominal walls in obese patients. He stressed its many advantages during and after operation on the upper abdomen, including the lessened likelihood of a postoperative hernia. In 1941, Cherney reported his modified transverse incision with separation of the rectus muscles from the symphysis. In 1946, Smith stated that the Cherney incision was readily adaptable to surgery of the bladder, diverticula, and lower ureters. Culp and DeWeerd, in 1953, discussed the advantages of the Cherney incision and stated that the "incision has inherent advantage which cannot be equalled by any other type of incision and . . . difficult pelvic urologic operations which so frequently confront the urologist can be performed with less wear and tear on both the patient and the surgeon if the Cherney incision is used."

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In 1955, Cherney reported on 808 surgical cases following detachment of the recti from the symphysis and pelvic bones. There were six (0.75%) wound disruptions and five (0.6%) postoperative hernias. He again pointed out the technical simplicity, adequate exposure, healing resulting in a strong abdominal wall, postoperative comfort, and cosmetically pleasing scar.

Fig. 1 (case 1).—Preoperative photograph showing large pendulous abdominal wall and large umbilical hernia (1955).

We first used a modified Cherney incision in 1945. In patients requiring a total cystectomy the tendinous rectus insertions were divided about 1 cm. above their insertion. There was difficulty in closing the modified incision, and the procedure was abandoned. Soon after Cherney's article appeared in January, 1955, a patient appeared in whom the Cherney incision seemed strongly indicated. The use of the Cherney incision simplified what would probably have proved a hazardous suprapubic prostatectomy with a complicating umbilical hernia.

Report of Cases

Case 1.—A man, aged 70, was admitted to Passavant Memorial Hospital on Feb. 12, 1951, with a history of gross hematuria four days before. Examination revealed an obese individual weighing 300 lb. (181.4 kg.) (fig. 1). The general physical examination was noncontributory except for discovery of a large umbilical hernia and an enlarged prostate, grade 2+. The blood pressure was 152/86 mm. Hg. The urine now was clear with an occasional red blood cell and white blood cell. A tumor of the bladder was suspected. We were unable to pass a cystoscope or a resectoscope. A cystogram revealed a filling defect on the bladder floor, possibly a middle prostatic lobe or neoplasm (fig. 2). The anterior urethral strictures responded to an indwelling catheter. The patient was readmitted to the medical service five times during the next four years for a weight reduction program. He was a connoisseur of foods and cooking and rapidly regained weight after each discharge from the hospital.

On Jan. 11, 1955, he was readmitted for gross hematuria and acute urinary retention. A futile effort was made to pass a long resectoscope through the site of a perineal urethrotomy. A suprapubic operation became mandatory. Because of the patient's large umbilical hernia, two of us performed the suprapubic prostatectomy. The Cherney incision was selected to avoid rectus muscle separation and encroachment upon the umbilical hernia. The pendulous abdominal wall was supported by two assistants during the operation. The Cherney incision proved ideal and allowed easy access to the bladder and enlarged prostate. A benign adenoma weighing 122 Gm. was removed. An indwelling catheter and drains were put in place, and the incision was closed by suturing the tendinous ends of the rectus muscles to the under surface of the fascia with fine interrupted silk sutures.

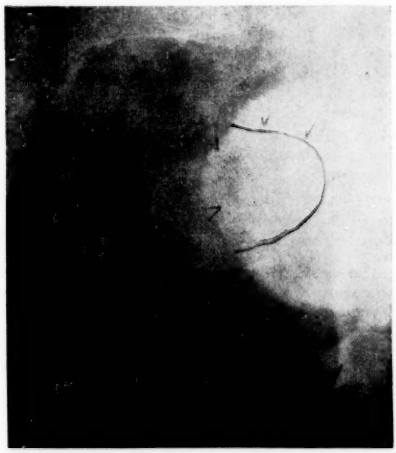

Fig. 2 (case 1).—Cystogram showing large tumor on floor of bladder encroaching on bladder outlet.

The abdominal fascia and skin were then likewise closed with interrupted silk sutures. The convalescence was uneventful, the wound healed well, and the abdominal wall

appeared strong. A checkup in June, 1957, revealed mild anterior urethral coarctations. The patient was still obese, asymptomatic, and enjoying retirement in a Florida atmosphere. The scar from the transverse incision was inconspicuous, the wound was well healed, and the wall was strong (fig. 3). The large abdominal hernia, now 24 cm. in diameter, remains asymptomatic.

There are many other pelvic urologic operations where maximum exposure is mandatory in order to reduce morbidity and facilitate the procedure; these include cystectomies, segmental bladder resections, reimplantation of ureters into the bladder, bladder fistula, bladder diverticula, seminal vesiculectomies, and radical prostatectomies. The Cherney incision has been used to marked advantage and with no untoward complications in conjunction with four recent radical retropubic prostatectomies. In case 2 is reported a radical retropubic prostatectomy for early carcinoma complicated by a symptomatic inguinal hernia on the left side. The hernia was repaired intrapelvically before the Cherney incision was closed.

Case 2.—A man, aged 69, admitted Jan. 13, 1957, complained of difficulty in voiding, small urinary stream, diuria, nocturia, and pain at the base of the penis. The general physical examination was noncontributory except for discovery of the grade 1 nodular prostatic enlargement and a

Fig. 3 (case 1).—Postoperative inconspicuous but strong transverse Cherney incisional scar and large umbilical hernia (1957).

symptomatic left inguinal hernia. The patient had had hernial repair on the right side in 1947 and a cholecystectomy in 1949. The medical survey revealed no contraindication to surgery. Intravenous pyelography revealed an intravesical prostatic enlargement, a renal cyst on the left, and no evidence of bone metastasis (fig. 4). The acid phosphatase level was 3.26 King-Armstrong units per 100 cc. The blood urea nitrogen level was 17.6 mg. per 100 cc., blood sugar level 77 mg. per 100 cc., and the blood cell count and differential normal. A transurethral biopsy and vasectomy were carried out. The microscopic sections showed adenocarcinoma of the prostate. It was thought that this patient's carcinoma was sufficiently confined to allow a radical prostatoseminal vesiculectomy.

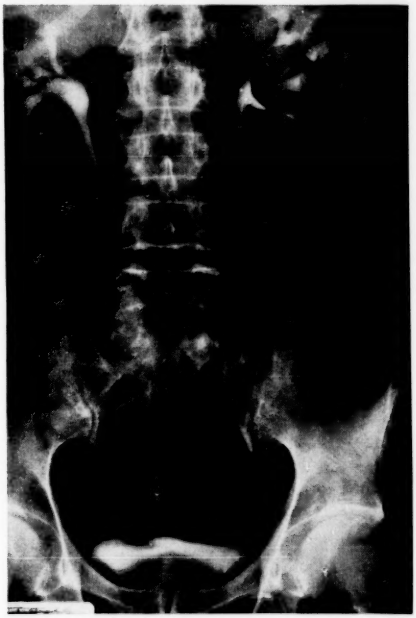

Fig. 4 (case 2).—Excretory pyelogram showing intravesical prostatic enlargement, asymptomatic left pyelographic defect suggesting cyst, and normal pelvis and lumbar spine.

On Jan. 28, 1957, the removal of the prostate and seminal vesicles was easily carried out by the retropubic approach through the Cherney incision. After the anastomosis of the bladder to the urethra, intrapelvic hernial repair was done by suturing the transversalis fascia to the adjacent periostium of the left pubic bone. The tendinous rectus insertions were resutured to the symphysis, and the remaining wound was closed with fine interrupted silk sutures. The patient made an uneventful recovery except for a perivesical abscess which developed on the right side three weeks after the operation. The infection necessitated surgical drainage. This increased his hospital morbidity. He was discharged on the 40th postoperative day with mild stress and strain incontinence. A follow-up study showed improvement in incontinence and no demonstrable evidence of residual carcinoma.

A fear still exists among urologic surgeons that division of the rectus insertions entails undue risk and postoperative wound disruption. When these wounds are healed, they are asymptomatic and the

walls are strong. When the insertions are attached to the abdominal wall fascia, as is possible with this incision, the sutures may be placed without undue tension. The pelvic exposure accomplished through the Cherney incision is unequalled by any other type of low abdominal incision. The incision allows comfortable access to the remote pelvic recesses in very obese patients. When indicated, intrapelvic hernial repair is feasible with the Cherney incision without increasing the operative morbidity.

Summary and Conclusions

The Cherney incision is extremely useful in urology for pelvic operations on the bladder, prostate, seminal vesicles, and urethra. In obese patients, it is the incision of choice for pelvic urologic operations. Wound healing is strong and is followed only occasionally by disruption and hernia.

720 N. Michigan Ave. (Dr. Riba).

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MEDIAN NEURITIS (CARPAL TUNNEL SYNDROME) CAUSED BY GOUTY TOPHI

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The syndrome resulting from compression of the median nerve at the wrist has been designated variously: median neuritis, median thenar neuritis, professional or occupational median neuritis, thenar neural atrophy, partial thenar atrophy, thenar palsy, tardy median palsy, median neuropathy, and, most commonly at present, carpal tunnel syndrome.

Recognition of this syndrome has evolved slowly. Paget [1] a century ago called attention to the late development of disturbed function of the median nerve after fractures of the wrist; this delayed, or tardy, median palsy was ascribed by him to compression of the nerve under the transverse (or volar) carpal ligament by the presence of callus or of thickened and indurated tissues adjacent to the nerve. In 1909, Hunt suggested that thenar atrophy might be caused by compression of the thenar branch of the median nerve as it emerged from beneath the transverse carpal ligament; later he attributed the lesion to compression of the median nerve beneath the ligament.[2] Marie and Foix [3] in 1913 and Moersch [4] in 1938 noted that the median nerve might be compressed beneath the transverse carpal ligament and suggested the possibility of treatment by section of that ligament. Woltman [5] in 1941 and, subsequently, Zachary,[6] Cannon and Love,[7] and Brain and associates [8] reported the successful treatment of median neuritis by means of surgical decompression of the nerve. Since then recognition of the condition has become more widespread and reports of its successful surgical treatment have been numerous.

As the syndrome has become known more generally, so too have increased the suggested causes of compression of the median nerve in the carpal tunnel: the late effects of major trauma,[1] occupational microtrauma,[2] acromegaly,[5] osteoarthritis,[9] nonspecific thickening of the transverse carpal ligament [10] or flexor tendon sheaths,[11] rheumatoid arthritis,[10] amyloid disease,[12] myxedema,[13] neuroma,[7] Léri's pleonosteosis,[14] anomalous artery,[9] impingement by a slip of the sublimis muscle,[9] carpal ganglion,[15] and idiopathic nocturnal swelling of the hands.[16] Rheumatoid arthritis with tenosynovial swelling about the flexor tendons at the wrist is one of the commoner causes of the carpal tunnel syndrome in our recent experience.

We have encountered a case of bilateral compression of the median nerve at the wrist with resulting neuritis, unique in that compression was caused by the presence of large urate deposits in and about the carpal tunnels.

Report of a Case

A 56-year-old man, seen at the Mayo Clinic in January, 1957, complained of pain, weakness, and numbness of the fingers of both hands during the preceding two years. In 1942, he had had his first attack of acute gouty arthritis, and shortly thereafter hyperuricemia was discovered. From 1942 to 1948 he had four more attacks of moderately severe acute gouty arthritis. In 1948, an unusually severe and prolonged attack involved the ankles and several joints of the feet. Subsequently, the ankles and feet had remained

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chronically swollen and painful; frequent attacks of acute gouty arthritis involved one or more joints, especially the metatarsophalangeal and tarsal joints, ankles, knees, wrists, elbows, and finger joints. Since 1950, tophaceous deposits had enlarged gradually on the flexor aspects of both wrists, on the ears, about the first metatarsophalangeal and various finger joints, in the olecranon bursae, and at the insertion of the Achilles tendon. In 1953 and again in 1954 large tophi had been excised from the region of the first metatarsophalangeal joints, left ankle, and both olecranon bursae. Both times the procedure had been followed by severe attacks of acute gouty arthritis. Prior to 1953 the patient had not followed prescribed treatment for gout, but since then he had been taking 0.5 Gm. of probenecid (Benemid) and 1/100 grain (0.6 mg.) of colchicine once or twice daily.

About two years preceding his visit to the clinic in 1957 the patient began to note intermittent numbness and tingling of the first four fingers of both hands and pain in those fingers and in the wrists, particularly when he used his wrists and fingers. The fingers, especially the thumbs, gradually weakened. Numbness and pain of the fingers and pain at the wrists worsened. He became almost incapacitated in respect to use of the hands.

The patient was moderately obese, and on physical examination numerous tophi of various sizes were seen on the ears and about the proximal interphalangeal and metacarpophalangeal joints, wrists, olecranon bursae, ankles, metatarsophalangeal joints, and the insertion of the Achilles tendons. The tophi on the flexor aspects of both wrists were 3-4 cm. in diameter. Muscles of the right thenar region were atrophic. Thenar, hypothenar, and interosseous muscles of both hands were slightly weak, those of the right hand being weaker than those of the left hand. There was hypesthesia in the distribution of the median nerve in the right hand.

Results of laboratory examinations were normal except as follows: concentration of uric acid was 10.2 mg. per 100 cc. of serum and roentgenograms of the wrists and hands showed evidence of osteoporosis, more marked on the right than on the left.

Electromyographic examination with a needle electrode did not reveal evidence of fibrillation or fasciculation in the right opponens pollicis and abductor pollicis brevis muscles. Voluntary contraction of these muscles evoked motor-unit potentials of normal size, but the number of these potentials from the right opponens and abductor pollicis brevis muscles was slightly reduced. Electric stimulation of the median nerves with a maximal stimulus for motor fibers yielded the following results: The amplitude of the action potential of the thenar muscles was just below the normal range in both hands; the latency of the response or "conduction time" between the moment of stimulation of the median nerve just proximal to the carpal tunnel and the beginning of the action potential of the thenar muscles was prolonged bilaterally, being 6.1 msec. on the right and 6.9 msec. on the left. The upper limit of normal is 5 msec. Conduction velocities of the median nerves from the elbow to the wrist proximal to the carpal tunnel were within the normal range.

Our diagnosis was bilateral median neuritis, or carpal tunnel syndrome, owing to compression of the median nerves by tophaceous deposits. On Jan. 17, 1957, the median nerves were decompressed by means of excision of tophi from the wrists and section of the transverse carpal ligaments (see figure). Bilaterally, there were a few tophi in the superficial tendons and extensive tophaceous deposits in the deep flexor tendons and tendon sheaths, with considerable fibrosis surrounding the tophi. A large mass of urate crystals, about the size of a golf ball, was located beneath the deep flexor tendons and above the interosseous membrane and pronator muscles bilaterally. The right transverse carpal ligament was greatly thickened by multiple tophaceous deposits, and the median nerves of both hands obviously were compressed by tophaceous masses. The pathologist found the excised masses to be composed of urate crystals.

After operation, a severe flare of acute gouty arthritis involved several peripheral joints; treatment with 25 grains (1.6 Gm.) of aspirin three times daily by mouth, colchicine, and dextrose administered intravenously was successful. After operation, the patient experienced a temporary slight increase in sensory loss and muscle weakness in the median distribution of the right hand; the left hand was normal in strength and sensation, although occasional paresthesias persisted. He was dismisssed on Jan. 30, 1957, at which time the operative wounds were healed. He was advised to follow a diet low in purine, to reduce his weight, and to take 2 Gm. of probenecid daily and 2 Gm. of sodium bicarbonate three times daily. Four months later he reported marked improvement in strength and sensation in his hands and was able to play golf for the first time in 18 months.

Comment

To the growing list of conditions recognized as causes of compression of the median nerve beneath the transverse carpal ligament, this case adds another, namely, gouty tophaceous deposits. Although tophi are seen more commonly in certain other locations, they do occur occasionally at the wrist. Undoubtedly other instances of the carpal tunnel syndrome caused by gouty tophi will be found if sought.

Findings at operation on right wrist: *X*, base of thumb; Y, median nerve; and Z, tophaceous mass. Transverse carpal ligament has been sectioned.

Proper treatment for gout with uricosuric agents and a diet low in purine may reduce the size of tophi, but the process often is prolonged and much fibrosis and tissue thickening may remain. Thus, to afford quicker and more certain relief of symptoms and to avoid possible permanent damage, surgical decompression of the nerve would seem advisable in instances such as the one here reported.

The following manifestations of compression of the median nerve at the wrist are characteristic when the syndrome is present in its overt form: pain, paresthesias and sensory deficit in the distribution of the median nerve in the hand, and

weakness and atrophy in muscles of the hand supplied by the median nerve, that is, the abductor pollicis brevis, the opponens pollicis, the superficial head of the flexor brevis pollicis, and the two lateral lumbricales. Loss of power of palmar abduction of the thumb may be more marked than weakness of opposition, since the adductor pollicis and part of the flexor pollicis brevis, which also aid opposition, are innervated by the ulnar nerve. Often the involvement of the nerve may be incomplete, thereby giving rise only to parts of the syndrome, particularly in early stages of development or in mild cases. For example, in the patient whose case is reported here the involvement on the left, although productive of distressing pain and paresthesias, was not accompanied by clinically apparent muscular atrophy or objective sensory loss. Likewise, anomalous and overlapping innervation may lead to certain variations. In a few instances, pain, apparently arising from compression of the median nerve at the wrist, has been noted to extend up the arm to levels as high as the shoulder.[17] Obviously, a careful neurological examination is required to distinguish median neuritis from protruded cervical disk, hypertrophic cervical arthritis, lesions of the brachial plexus, thoracic outlet syndrome, and generalized polyneuritis.

The following confirmatory signs of median neuritis aid in making the diagnosis: Tinel's sign, that is, tingling in the median distribution produced by tapping over the median nerve at the wrist; increased pain in the median distribution as a result of acute flexion or extension of the wrist or temporary ischemia of the extremity; and palpation of a tender swollen median nerve just above the transverse carpal ligament. We have found electromyography and measurement of the conduction time in the peripheral portion of the median nerve to be of particular diagnostic help; the characteristic findings are those of prolonged conduction time from the wrist to the thenar muscles and evidence of denervation in the muscles of the hand supplied by the median nerve.[18] As this case illustrates, prolonged conduction time may be present when signs of denervation are minimal or absent.

Summary and Conclusions

In a unique instance of bilateral median neuritis (carpal tunnel syndrome) caused by compression from gouty tophi, treatment by surgical excision of the tophi and sectioning of the transverse carpal ligaments was successful. Surgical intervention affords quicker and more certain relief than might be expected from treatment with uricosuric agents and seems to be the treatment of choice in a case of this sort. Electromyography, including measurement of the conduction time from wrist to thenar muscles in the median nerves, is an especially helpful diagnostic aid in instances of the carpal tunnel syndrome. The carpal tunnel syndrome is particularly likely to occur in patients who have some arthritic or rheumatic affliction at the wrist, such as rheumatoid arthritis, idiopathic tenosynovitis, osteoarthritis (especially post-traumatic), and, as illustrated, gouty tophi.

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Electromyographic examination and electric stimulation of the nerves were performed by Dr. E. H. Lambert.

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REGIONAL BLOCK AT THE WRIST OF THE GREAT NERVES OF THE HAND

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"Local anesthesia" is a term often mistakenly used to include all methods of anesthetization not included under general, topical, or spinal. There are two still-popular traditional techniques by which local anesthetics are administered: 1. The rapid insertion of the needle followed by a swift injection of all the solution that the tissues can take (fig. 1, *A*). This is used for the performance of elective procedures on the body. Quite often, one seeks for paresthesias in the nerves prior to injection. 2. The second popular method, based on equally fallacious reasoning, is used for the repair of open wounds. After the patient has suffered cleansing of the wound with tincture of green soap or one of the modern germicidal soaps (both of which cause pain), the wound is infiltrated by multiple insertions of the needle both in the proximal and distal wound edges (fig. 1, *B*).

There are several fallacies in these techniques. First, the hydrodynamic pressure of great quantities of fluid is not required to arrest nerve fiber conduction. Only enough solution is needed to bathe the nerve. Second, rapid insertion of a needle is needed to minimize pain only when the needle is large. The proper use of a tiny, no. 25 needle results in no pain when it is inserted slowly. Third, rapid pumping up of the tissues is painful. A slow injection of small amounts of solution causes no pain. Fourth, it is technically safer to inject through prepared intact skin away from the wound than through the

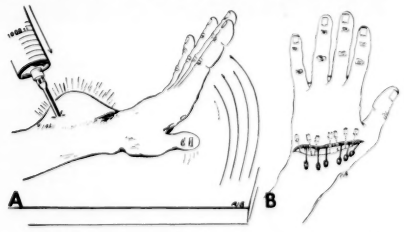

Fig. 1.—Traditional techniques for injection of local anesthetic for *A*, elective surgery, and *B*, surgery of injury due to trauma.

raw tissues in the wound site. Fifth, cleansing of a wound with solutions that cause severe pain also causes concomittant severe tissue damage in addition to the original trauma. Cleansing a wound with anything prior to anesthetization causes pain and is therefore cruel. It is painless and far more humane to inject just once proximal to the wound than to inject many times into the tissues.

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Regional Block Anesthesia

A more proper use of local anesthetic solutions, from bacteriological, surgical, pharmacological, and humane viewpoints, could be summarized as follows: (1) complete anesthesia for more than the site of surgery, to ensure that no part of the operative procedure shall cause pain in unanesthetized tissue; (2) painless injection; (3) bacteriologically safe site of injection; (4) use of minimal amount of solution to avoid compression of vascular and lymphatic tissue; and (5) avoidance of injection into nerves.

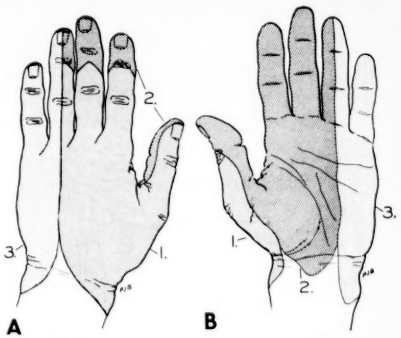

Fig. 2.—Distribution of sensory nerves in the hand. *A*, usual dorsal distribution, and *B*, usual volar distribution.

When only one digit need be anesthetized, the digital nerves are blocked in the palm and beneath the dorsal skin.[1] When more than one digit is to be anesthetized and the surgical procedure does not require the use of a tourniquet, I have found it most convenient for patient and surgeon to establish a regional block of the proper nerves to the hand at the wrist.

The proper use of a tourniquet in surgery of the hand indicates its placement high up on the upper arm. The traditional use of a rubber band or a piece of rubber tubing clamped with a hemostat as a tourniquet at the base of the finger is not only unnecessary but dangerous. If bleeding is arterial in a minor laceration, it may be stopped with pressure of a sterile sponge. If it commences again during soap and water cleansing, it will usually be of

less magnitude and, in my experience, may be left untouched until cleansing is complete when digital pressure at the sides of the finger will arrest its flow so that the artery may be carefully clamped in a relatively sterile field under unimpeded vision.

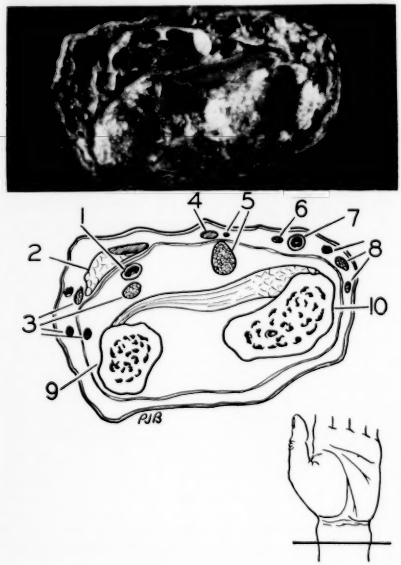

Fig. 3.—*Top*, cross-section of wrist just proximal to styloid processes of ulna and radius. *Bottom*, diagram of cross-section: (*1*) ulnar artery, (*2*) flexor carpi ulnaris, (*3*) ulnar nerve and its branches, (*4*) palmaris longus tendon, (*5*) median nerve and its branch (variable), (*6*) anterior branch of lateral cutaneous nerve of forearm (variable), (*7*) radial artery, (*8*) branches of radial nerve, (*9*) ulna, (*10*) radius.

If trauma is extensive and bleeding profuse, direct pressure should be applied and the reparative procedure carried out in the operating room with a tourniquet high on the upper arm and a higher block [1A] or a general anesthetic.

The indications for regional block at the wrist are lacerations of the skin, skin grafts, and fractures. The contraindications may be summed up under the general heading of those conditions the treatment of which require a bloodless field with a tourniquet on the upper arm, such as injuries to tendons and nerves and severe crushing injuries.

Anatomy

In figure 2 is outlined the sensory distribution of the three nerves to the hand. Their boundaries must not be considered to be so sharply circumscribed as indicated because there is much variation in dorsal sensory nerve distribution and some overlapping of volar nerve distribution.[2] Therefore, it is discrete for the surgeon to plan to anesthetize not only the projected field of surgery but also a goodly margin about it. Another reason, too, for establishing a broad area of anesthesia is that occasionally the surgical procedure covers a larger field than anticipated.

Figure 3 shows a cross-section of the wrist just proximal to the styloid processes of the radius and ulna. There are several anatomic points to be noted here in order to simplify the anesthetization of these nerves.

First, the three nerves are no longer single nerves but have already ramified. The median nerve has sent off a variable tiny slip to the subcutaneous tissues. The ulnar nerve has divided beneath the volar fascia of the wrist and has also sent off some subcutaneous branches. The radial nerve is entirely superficial to the fascia.

Second, each nerve and its branches are either just within a relativeiy large fascial enclosed compartment or just superficial to a layer of fascia (subcutaneous). This fact makes for easy and sure anesthetization of each nerve without the need for eliciting paresthesias and without pumping the spaces full with ounces of anesthetic solution. This, plus the easily identified landmarks as shown be-

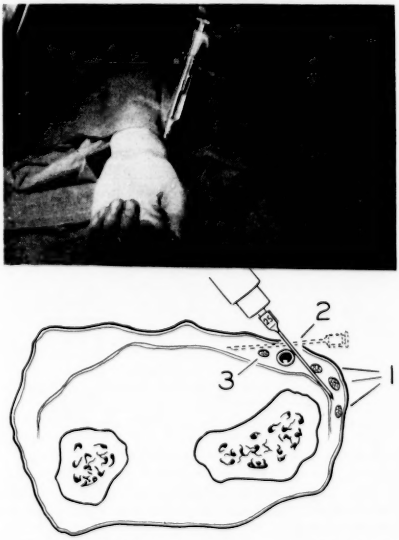

Fig. 4.—Anesthetization of radial nerve at wrist for elective procedure on thumb: (*1*) branches of radial nerve, (*2*) radial artery, (*3*) anterior branch of lateral cutaneous nerve.

low, promotes the successful bathing of each nerve with anesthetic solution, which is followed by complete arrest of nerve impulses.

Technique

I have used 2% solution of lidocaine (Xylocaine) hydrochloride with a 1:200,000 concentration of epinephrine in the uniformly successful initiation of anesthesia for 38 blocks of one or more nerves at the wrist in the past year. A 2-ml. syringe suffices for the block of one nerve or a 5-ml. syringe for the blocking of two nerves. A $\frac{5}{8}$-in. no. 25 needle is used for all blocks. No wheals are made. If paresthesias are felt by the patient, the site of the needle point is changed.

There is never any sign of the solution having been injected until several minutes after, when an occasional surface lymphatic may have picked up some lidocaine and epinephrine; this is manifested by the appearance of some white lines in the skin of the forearm. A 10-minute wait results in complete anesthesia. The anesthesia lasts for at least two

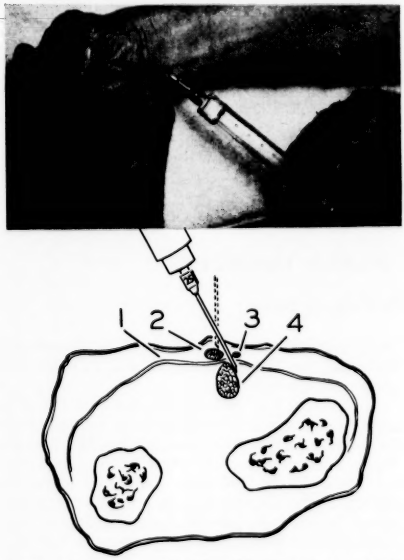

Fig. 5.—Anesthetization of median nerve at wrist for fingertip injuries (lesions are usually kept covered until anesthesia is complete; they are then cleansed): (*1*) volar antebrachial fascia, (*2*) palmaris longus tendon, (*3*) superficial branch of median nerve, (*4*) median nerve.

hours. Any procedure on the hand that requires more than one hour is probably of such magnitude as to require a tourniquet and, consequently, a higher block.

Radial Nerve Block.—To produce a radial nerve block, the radial artery is first palpated (fig. 4). The point of the needle is gently placed just into the skin directly over the artery, where an imperceptible amount of solution is deposited. After a hesitation of a few seconds, the needle is pressed

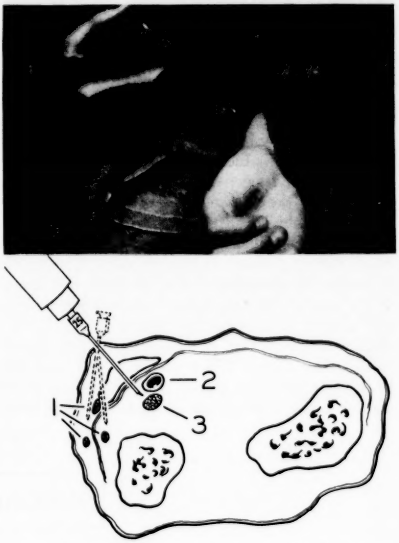

Fig. 6.—Anesthetization of ulnar nerve for elective procedure on distal palm: (*1*) branches of ulnar nerve, (*2*) ulnar artery, (*3*) ulnar nerve.

through the skin into the subcutaneous fatty tissue, where a few minims of solution are deposited. The needle is then angled dorsally nearly parallel to the skin and is pushed through the fat to its entire length. Here the plunger is withdrawn slightly to test whether the needle is in a vein. If it is not in a vein, 1 ml. of solution is injected. Another 0.5 ml. is injected as the needle is withdrawn to its initial position, with its point just over the artery, when it is angled volarward. Again it is pressed in to its entire length and the remaining 0.5 ml. is deposited as it is withdrawn.

Median Nerve Block.—Note in figure 5 that there is a tiny superficial slip of the median nerve lying in the fat to the radial side of the palmaris longus tendon. The main part of the nerve lies beneath the volar fascia, either beneath or just to the radial side of the palmaris longus tendon. The top picture in figure 5 shows how the patient flexes his wrist against counterpressure with his fingers and thumb straight. This maneuver brings his palmaris longus

and flexor carpi radialis tendons into sharp relief. If the wrist is fat, the tendons can be easily palpated. The needle is gently inserted into the skin and then into the subcutaneous fat (as was done for the radial nerve) directly over the palmaris longus tendon.

When the subcutaneous injection has been made, the needle is drawn to the radial side of the tendon, moving the loose skin with it. Here the needle is pressed deeper until it strikes the firm resistance of the volar fascia, where 0.5 ml. of solution is deposited. After a brief hesitation, firm gentle pressure pushes it through this layer with a definite sensation that is easily felt. The entire bevel of the point must go through the fascia, but the needle must not be pushed deeper for fear of impaling the nerve. Here, the remaining 1.5 ml. of solution is deposited and the needle removed.

Ulnar Nerve Block.—To produce an ulnar nerve block the ulnar artery is first palpated. The needle is pressed on through the skin, as above, just lateral to the artery. After the subcutaneous injection of a few minims of solution, the needle is pushed in a medial direction (fig. 6, diagram) to pass lateral to the ulnar artery. When the point has been felt to traverse the volar fascia, it is pressed on about another ¼ in., where 1 ml. of solution is deposited.

The needle is then withdrawn until the point is in the subcutaneous fat, when it is angled more dorsally and again pushed through the fascia. Another 0.5 ml. of solution is deposited in the event that there is a small branch from the main part of the nerve. The needle is again withdrawn until its point is in the subcutaneous fat, where it is angled dorsally so as to remain in the fat. It is pushed in to its full length, and the remaining solution is deposited along its tract as it is withdrawn.

Summary

The technique of regional block anesthesia of the nerves at the wrist has been employed in 38 consecutive successful blocks of one or more of these nerves in the past year. Each site of injection is easy to identify. The nerves to be anesthetized at each site are within fascial sheaths or are subcutaneous, which assures bathing the nerve with anesthetic solution without the necessity of eliciting traumatizing paresthesias.

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SPECIAL ARTICLE

DOCTOR'S MANUAL OF SPEECH DISORDERS

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Because the family physician, or the pediatrician, is almost always the first one to be contacted by the parents of a child with a speech problem, real or imagined, it is essential that the doctor know what constitutes a speech problem, what to do about it, or where to refer it. To help the doctor to give adequate advice to the family with a speech problem, the following discussion is presented.

Normal Development of Speech

In order to understand when speech is deviating from the normal and the nature of the deviation, it is necessary first to understand the normal development of speech. With an understanding of how speech develops, it is not difficult to evaluate the speech of a child by the time he is a year old. At any particular age thereafter it can be determined when the development is abnormal to a degree that constitutes a problem.

In assessing the prelanguage development of a child in its first year, one needs to be aware of how the child vocalizes, what sounds he makes, how he begins to combine sounds, when and how he develops vocal variety (inflection), when he begins to imitate, and when and how he responds to spoken sound. Between the ages of 1 and 6, children quite consistently follow a general pattern in development of expressive speech, comprehension of speech, articulation of sounds, general intelligibility, and sentence structure. The language development charts in tables 1, 2, and 3 show, in abbreviated form, the normal pattern of language development from birth to age 6. Some deviations can be expected at times and should be taken into account. Unusual deviations may indicate trouble and the necessity to do something about it.

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Critical Periods in Speech Development

Many parents and some doctors appear to feel that the first year of a child's life is relatively unimportant with respect to the growth and development of language because little speech appears. The fact is, however, that this period is extremely important. A great deal of prelanguage activity takes place from the time the child begins actively to babble, at the age of about 4 months, until he begins to use his first words some time between 9 and 12 months. The babbling appears to be a rehearsal for the first words. It is that period in which the child learns to enjoy hearing and making a variety of vocal sounds. Because he enjoys this activity, he does a great deal of it. In so doing, he makes many different sound combinations, which provide some valuable ear training as well as exercise of the speech organs.

Because baby enjoys playing with sounds, others around him join in the fun and repeat the sounds back to him. Mother is likely to take her cue from the baby during this period and babble with him. Through this method he comes to know that the making of sound has an effect on others. He begins to use it for this purpose. At this point, usually 9 to 12 months, he will begin to vary his pitch, inflection, and volume to suit particular needs. At the same time, he will be making combinations of sounds that begin to sound like words. In this manner, the combination "mama" usually appears. Mother hears it and usually comes to baby, repeating "mama" after him several times. It does not take long for baby to learn that repetition of this particular combination of sounds will satisfy many of his needs. Other words develop in the same way, and a vocabulary is begun.

Normal development of language can be interrupted in the first year by events that might interfere with baby's vocal play and prelanguage activity. Prolonged or serious illnesses, congenital malformations, birth trauma, delayed general development, mental retardation, or inadequate hearing may affect the child in such a way as to prevent babbling and the enjoyment of prelanguage activity. Emotional trauma, even during the first year, also can interfere with language development. The lack of a mother, or a mother figure, in close rela-

TABLE 1—*Pattern of Normal Language Development in Vocalization and Response to Vocal Sound*

Age, Mo.	Vocalization	Response to Vocal Sound
1	Crying, whimpering, produces some vowels and consonants, k, g, h. Sighs, grunts, explosives.	
2 and 3	Pitch of crying slightly higher. More nonerying vocalizing. Different kind of crying for pain, hunger. Some repetitive vocalizing, "gagaga." Adds m, ng.	Sometimes smiles or is soothed by pleasant adult voice. Responds to adult cooing by repeating own formerly practiced sounds. Sometimes stops vocalizing when adult joins in. May cry in response to angry voice; coo, sigh, gurgle in response to pleasant voice.
4	Babbling and vocal play begins, repetitive vocalizing—mostly when child is alone. Begins to use consonants m, k, g, p, b, ng, and most vowels. Smiles, laughs, gurgles, coos when comfortable.	Imitative response to speech decreases and does not reappear until about the ninth month. Indiscriminate interruption of babbling causes child to stop vocalizing.
5	Increase of above. Occasionally responds to parental babbling if done softly and not interrupting child's vocal play.	Responds to voices by turning eye and head. Automatic response to friendly or angry tone. Vocalizes displeasure at losing toy, etc.
6	More repetitive babbling, with marked rhythm. Increase in intensity from whisper. More nonerying sounds. Nasal tone begins to be heard. Some tongue-tip activity begins.	Response to friendly or angry tone not automatic but depends on other aspects of the situation: gestures, physical contact.
7	More variety. Dissyllables. Same sounds repeated several days. Adds d, t, n, w to babbling.	Mostly rejects demands for imitation of sounds. Responds to gestures accompanied by voice.
8	Begins to imitate own vocal play, "mama," "dada," "baba" but not in response to adults. Babbling shows pitch and inflection change. Increased tongue-tip activity.	Calls for attention. Combines babbling with gestures. Perseverates in imitating hand clapping, etc., accompanied by voice.
9	More variety in crying and babbling, more back vowels used. Higher pitch and more pitch variation. Crys to get attention. More of vocalizing is babbling rather than crying.	Retreats from strangers and mostly from other children by crying. Holds out arms to be picked up if adult does the same. Not much imitative response to accompanying vocalizing.
10	Makes effort to imitate others. Can imitate if adults use same sounds as in child's vocal play. May use one word correctly.	Begins to comprehend "no no," "dada." Will respond to words "patty-cake," "bye bye," with gestures.
11	Can imitate correct number of syllables and sounds heard in adult vocal stimulation. Imitates some new sounds not previously used.	Shows interest in isolated words associated with objects or activities important to the child. Will imitate two tones sung by an adult.
12	Some echolalia if sounds introduced unobstrusively by adults. Accompanies vocalization with gestures. May acquire first true word(s). Much interest in isolated words connected with own needs and activities.	Sometimes will imitate dogs, clocks, cows, or adult exclamations. Imitates adult words with initial sound(s). "Pup" —"p" or "pu." Often imitates dissyllabic words.

TABLE 2.—*Pattern of Normal Language Development in Articulation and General Intelligibility*

Age, Yr.	Articulation	General Intelligibility
1-2	Uses all vowels and consonants m, b, p, k, g, w, h, n, t, d. Omits most final consonants, some initial. Substitutes consonants above for more difficult. Much unintelligible jargon around 18 mo. Good inflection, rate.	Words used may be no more than 25% intelligible to unfamiliar listener. Jargon near 18 mo. almost 100% unintelligible. Improvement noticeable between 21 and 24 mo.
2-3	Continues all sounds above with vowels but use is inconsistent. Tries many new sounds, but poor mastery. Much substitution. Omission of final consonants. Articulation lags behind vocabulary.	Words about 65% intelligible by 2 years; 70-80% intelligible in context by 3. Many individual sounds faulty but total context generally understood. Some incomprehensibility because of faulty sentence structure.
3-4	Masters b, t, d, k, g, and tries many others including f, v, th, s, z, and consonant combinations tr, bl, pr, gr, dr, but r and l may be faulty so substitutes w or omits. Speech almost intelligible. Uses th inconsistently.	Speech usually 90 to 100% intelligible in context. Individual sounds still faulty and some trouble with sentence structure.
4-5	Masters f and v and many consonant combinations. Should be little omission of initial and final consonants. Fewer substitutes but may be some. May distort r, l, s, z, sh, ch, j, th. No trouble with multisyllabled words.	Speech is intelligible in context even though some sounds are still faulty.
5-6	Masters r, l, th, and such blends as tl, gr, bl, br, pr, etc. May still have some trouble with blends such as thr, sk, st, shr. May still distort s, z, sh, ch, j. May not master these sounds until age 7½.	Good.

tionship with the child often seriously retards the development of speech. It is interesting that most children seem to have to go through the various stages of language development, including the early prelanguage period, no matter how late they start to talk. Even a 4, 5, or 6 year old who has had no speech often will begin, if he begins at all, by babbling. For this reason it is essential that the first year be conducive to normal prelanguage activity if later language functions are to develop according to schedule.

From the age of 12 to 18 months little obvious language development takes place. The child seems to be too busy learning to walk and to physically explore his immediate environment to be concerned with verbal explorations. During this period speech sometimes comes to a virtual standstill. Parents may become quite alarmed at this change and want to know the reasons for it. Normally, around 18 months the child's language begins to develop rapidly. From 15 to 20 words at 18 months, the expressive vocabulary may jump to 250 words by the time he is 2 years old. Some time during this period the child will pass through the "jargon stage" in which his speech will sound very much like normal well-inflected conversation, except that almost none of it is intelligible. This stage seems to be a rehearsal for the connected speech which should begin about the age of 2. Parents sometimes are alarmed at this 18-month jargon and think that something has gone wrong with the child's speech. They can be assured that he will pass through this stage quickly to the next one, in which he will begin to use connected speech in partial sentences such as "Go bye bye," "Baby go," "Daddy come."

TABLE 3.—*Pattern of Normal Language Development in Expressive Speech and Comprehension of Speech*

Age, Yr.	Expressive Speech	Comprehension of Speech
1-2	Uses 1 to 3 words at 12 mo., 10 to 15 at 15 mo., 15 to 20 at 18 mo., about 100-200 by 2 yr. Knows names of most objects he uses. Names few people, uses verbs but not correctly with subjects. Jargon and echolalia. Names 1 to 3 pictures.	Begins to relate symbol and object meaning. Adjusts to comments. Inhibits on command. Responds correctly to "give me that," "sit down," "stand up," with gestures. Puts watch to ear on command. Understands simple questions. Recognizes 120-275 words.
2-3	Vocabulary increases to 300-500 words. Says "where kitty," "ball all gone," "want cookie," "go bye bye car." Jargon mostly gone. Vocalizing increases. Has fluency trouble. Speech not adequate for communication needs.	Rapid increase in comprehension vocabulary to 400 at 2½, 800 at 3. Responds to commands using "on," "under," "up," "down," "over there," "by," "run," "walk," "jump up," "throw," "run fast," "be quiet," and commands containing two related actions.
3-4	Uses 600-1,000 words, becomes conscious of speech. 3-4 words per speech response. Personal pronouns, some adjectives, adverbs, and prepositions appear. Mostly simple sentences, but some complex. Speech more useful.	Understands up to 1,500 words by age 4. Recognizes plurals, sex difference, pronouns, adjectives. Comprehends complex and compound sentences. Answers simple questions.
4-5	Increase in vocabulary to 1,100-1,600 words. More 3-4 syllable words. More adjectives, adverbs, prepositions, and conjunctions. Articles appear. 4,5,6 word sentences, syntax quite good. Uses plurals. Fluency improves. Proper nouns decrease, pronouns increase.	Comprehends from 1,500 to 2,000 words. Carries out more complex commands, with 2-3 actions. Understands dependent clause, "if," "because," "when," "why."
5-6	Increase in vocabulary to 1,500-2,100 words. Complete 5-6 word sentences, compound, complex, with some dependent clauses. Syntax near normal. Quite fluent. More multisyllable words.	Understands vocabulary of 2,500 to 2,800 words. Responds correctly to more complicated sentences but is still confused at times by involved sentences.

The period from age 2 to 4 probably is the most critical with respect to language development. In this period the child makes a great effort to use his rapidly increasing, but very new and inadequate, vocabulary to meet his growing needs—and also to conform to a very confusing language environment. Often he finds himself without words at his command, so he does as any of us do in such a situation—he hesitates, sometimes backs up, sometimes repeats or fills in with "ah, ah, ah" or "I, I, I, I," and occasionally he will really block and give up the attempt to speak at that particular moment. This situation sometimes results in considerable nonfluency, which is quite normal for many children at this age. It appears much more readily, and usually lasts longer, in boys than in girls. Normally, if the speech is left alone, a child should pass through the worst of the nonfluency in about six months, but some will take from one to two years.

The danger in this situation comes not from the fact that the child is nonfluent but from the fact that adults—and sometimes other children—become disturbed and begin to treat the nonfluency as a problem. Adults often are ready to label this kind of speech as "stammering" or "stuttering." Once they do, they begin to treat the child according to the label. From here on they rapidly make a problem for him. They do this by such admonitions as "slow up," "stop and start over again," "don't talk so fast," "now think what you are going to say." Adults more unwise than this will even scold the child for his nonfluency, while some go so far as to punish him because he "doesn't talk right."

Usually it is during this period that the parents become worried and come to the doctor for help, with some such statement as "My Johnny is stuttering (or stammering). What shall I do?" Generally, the doctor's advice here has been good, in that he has told them to leave the speech alone. The parents, however, often are too disturbed to take this advice unless they have an adequate explanation of why they should leave the speech alone and how to leave it alone. It will help a great deal if the doctor can give them this explanation. The parents need to understand that this is a normal stage of speech development and that too much interference with it—even though the parents are trying to help—may result in a real speech problem. It would be well, too, if the parents and doctors did not label this nonfluent speech as stuttering or stammering. It can be described as "developmental nonfluency" or some other term that is not so fearful to parents.

Between the ages of about 3 and 6 years, a common hazard to the child's speech is that of parents, and others, expecting too much from him as far as the articulation of sounds is concerned. It is not uncommon for parents to become quite disturbed if the 3, 4, or 5 year old is not using the r, l, th, s, z, sh, ch, and some consonant combinations correctly. A glance at the preceding language development chart will show that these sounds all normally develop after age 5, and the last four may not be mastered until age 7. The danger in this situation is the possibility of pressuring the child to produce these sounds and others ahead of schedule and often before he is ready to produce them. Problems of reverting to baby speech, stuttering, and dyslalia sometimes result from this kind of pressure. The doctor can be most helpful here by informing parents as to the normal sequence of sound development and encouraging them to be patient and give the child time. The doctor should, however, know which sounds are in question and whether there is a problem. One of the pamphlets for parents might be suggested to parents with this kind of a question.

By the time a child is ready to start school, his language generally is adequate for most situations. A few children, however, have not gained sufficient stability in the use of language by the time they start school. They suddenly find themselves among 30 or 40 strange children and a strange adult. The language that previously has served them well among their family and a few friends now may be inadequate to cope with the much wider demands. The child again may become nonfluent just as he did during the earlier stage. Many cases of stuttering seem to have begun during kindergarten or first or second grade. The situation is exactly the same, and should be handled the same, as in the 2 to 4 year period. The nonfluency should not be labeled. The child should be given as much security and as little stress as possible while he is given time for his language to mature.

Another danger also is present at this period. Many children are not quite mature enough, in language behavior and in the use of the articulators, to be able to pronounce all sounds clearly by the time they start school. Actually, some do not achieve this maturity until 7 or 8 years of age. Many parents and teachers, however, become quite disturbed if the child is not producing all sounds correctly by the time he is ready to enter school. In order to get the child ready for school, they may begin to "help" him, to correct him, nag at him, and in other ways make a problem where there was no problem. The doctor can encourage the parents to give the child time to mature without expecting more than he is capable of producing. Of course there are speech deviations at any age which are not of a developmental nature and should have attention. The doctor will need to know how to recognize these and deal with them.

Deviations from Normal Speech

The speech pathologist thinks of a speech disorder in terms of its probable origin; either as organically caused or one that he calls functional (with no apparent organic cause) or a combination of both. These disorders usually are thought of as falling into one or more of four areas: 1. Articulation is the production of sound and sound combinations. Deviations in articulation account for from 50 to 70% of all speech disorders. 2. Stuttering (or stammering) accounts for about 25% of all speech problems and usually is broken down into primary and secondary stages, the latter being the stage at which the individual himself considers his nonfluency to be a serious problem. 3. Voice includes about 10% of all speech disorders, and refers to the processes of phonation and resonation and includes deviations of pitch, quality, or volume. 4. Symbolization refers to a language disturbance most usually called "aphasia" or "dysphasia." It is the inability to associate meaning with language symbols in a normal manner. It is thought that from 2 to 4% of speech problems may fall into this category.

The speech pathologist, in his diagnostic report, often will use other terms such as delay (one or more aspects of language, such as articulation, vocabulary, or structure, has not developed according to chronological age); dyslalia (articulation disorder due to structural anomalies or impaired hearing or "functional" causes); dysarthria (articulation disorder due to central nervous system damage affecting speech organs); dysphonia (disorder of voice quality, pitch, or volume); dysphasia (defined under "symbolization" above); rhythm (stuttering, stammering, or cluttering); hypernasality (too much nasal resonance); and hyponasality (too little nasal resonance).

Conditions Which Commonly Cause Speech Disorders

Late Physical Development.—Late physical development may cause retarded coordination and faulty function of the speech organs and two kinds of speech problems: (1) a delay in developing intelligible speech; and (2) articulatory distortion which may or may not follow the retarded speech pattern. In such cases, it is essential to establish the child's general developmental age. Speech therapy applied too early, for the late-developing child, might cause emotional problems and do little to remove the speech defect. Usually best results are obtained from speech therapy when the child is functioning mentally and physically at about a 4-year level.

Dental Misalignment and Malocclusion.—Dental misalignment and malocclusion are most likely to cause articulation problems such as distortion of the sibilant sounds, particularly s and sh. Correction of the structure by an orthodontist is the most direct remedy, but speech therapy often is needed immediately after the structure has been corrected.

Cleft Lip and Palate.—The problem of cleft lip and palate is generally threefold: 1. There is likely to be a retardation because the consonant sounds (p, b, t, d, k, g) needed by the child to establish his early vocabulary are the ones most disturbed by the open palate. Because of this, much of the prelanguage activity is omitted and early vocabulary and sound discrimination are faulty by the time the palate is closed. 2. With a soft-palate cleft, there is generally a hypernasal quality, even after surgery, due to insufficient closure in the velar-pharyngeal area. 3. Often there will be an articulatory problem caused by dental malformation or by faulty tongue placement which develops before the palate is closed.

Early counsel and instruction in speech development are essential for the parents of children with cleft palate. The speech pathologist should see the child and his parents within the first four months and about every six months thereafter for the first two years. It has been found that most of the delay in speech can be prevented under such a program. The original palate surgery sometimes is adequate to prevent hypernasality, but there is not always a close relationship between the length and flexibility of the palate and the degree of hypernasality. It has been found that a small nasopharyngeal leak will produce as much hypernasal quality as a large opening. "Pharyngeal flap" and "pushback" surgical procedures have been found effective in many cases. Dental intervention often can remove articulation problems due to faulty dental structure. Speech therapy, if needed, generally is desirable when the child with a cleft palate is about 4 years of age.

Complete or Partial Paralysis of the Speech Organs.—This condition may result from any disease or accident causing injury to the central nervous system. The speech problems are likely to be faulty articulation, inadequate voice quality, inadequate pitch, rate, or volume, or any combination of these. With this kind of problem the speech therapist can achieve best results in cooperation with the family doctor, the physical therapist, and the occupational therapist. In children with poliomyelitis it also is extremely important that the retraining program begin as soon as possible after the attack. The first six months appear to be the most critical as far as making adequate progress in speech is concerned. Therapy often must continue over a long period of time, and frequently the therapist must be satisfied with a minimum of progress. It has been found that from 50 to 60% of children with cerebral palsy will have severe speech problems. They are most common in the athetoid and are often accompanied by hearing loss, but the prognosis is usually quite good if the athetosis is not too severe.

"Brain Damage."—As used here the term "brain damage" is limited to central nervous system lesions in areas of the brain most directly affecting language functions and behavior. This kind of damage is associated with what has been called a "brain damage behavior syndrome," which is characterized by hyperactivity, disinhibition, catastrophic reactions, and generally deficiency in language and number concepts.

Speech problems resulting from brain damage, which may not be physically crippling, usually show a disturbance of the language-symbol association function. The most common result is an expressive (sometimes called motor) aphasia, in which the child can understand language but cannot reproduce it. More severe is the receptive (sometimes called auditory) aphasia, the inability to perceive and interpret language symbols. Often there is a combination of the two, called mixed aphasia. Most severe is global aphasia, in which both receptive and expressive areas are completely defective, and there appears to be no "inner language." In mixed and global aphasia all of the language functions are damaged and, if the child develops language, not only will his articulation be faulty but his language structure, vocabulary, and ability to read and write also are likely to be faulty. It is impossible to locate exactly a lesion in the brain from the type of language behavior observed. It is known, however, that a lesion in the left hemisphere generally will be found when the language function has been seriously interfered with. A lesion in the right hemisphere only rarely produces an aphasic condition. It sometimes is found that a major right hemisphere lesion, with some probable damage extending into the left hemisphere, will cause aphasia. It is fairly well established that expressive aphasia comes most often from a lesion in "Broca's area" in the frontal lobe of the left hemisphere. Reading, writing, and visual perception deficiencies also can be localized to about the same extent.

Considerable progress has been made in understanding aphasia in adults, but less is known about what seems to be a similar condition in children. It is felt that many children fail to develop language as they should because of brain lesions that have been undetected but probably were present at birth or occurred in early childhood. A number of children learn to communicate orally with fair adequacy, but unusual language dysfunction begins to show up when they try to learn to read and write in school. Some of these problems can be traced back to brain lesion. Therapy for either verbal or written dysphasia is an extremely complicated procedure, and the prognosis is always open to question. Excellent results have been obtained, however, in a number of cases. Adequate diagnosis is difficult and requires an experienced team of specialists but is of paramount importance.

Mental Retardation.—Mentally retarded children often present a picture of retarded language development with the retardation showing in all areas of language. This generally varies with the intelligence

level, however. Children whose intelligence level falls within the 80 to 90 IQ range are likely to develop adequate language unless other retarding factors such as physical and psychological problems are present. When the IQ level is between 70 and 80, it is not uncommon to find retardation in several areas of language. It has been found that most children with IQ's below 70 will develop language which is noticeably deficient in all areas. Improvement in language for the mentally retarded usually is a developmental and maturational process rather than a problem of therapy, although therapy may be justified in some cases. Parents, however, often feel that if the child "could just talk better" he would be all right. Consequently they insist on speech therapy or some other "treatment." The doctor can do much to help the family understand the nature of this problem.

Hearing Loss.—The nature of the speech disorder resulting from hearing loss depends largely upon the amount of loss and the child's ability to cope with it. Deafness or near deafness will cause a great delay in developing language, and faulty articulation, inflection, and pitch patterns will be present when it does develop. Less severe hearing loss is likely to result in articulation problems, particularly with respect to the high frequency sounds, the voiceless sounds, word endings, and sometimes initial consonants. It is not difficult to detect severe hearing loss, but the child with a borderline hearing loss often suffers from a misunderstood speech or behavior problem. In this child the loss is great enough to distort or eliminate many sounds but is not severe enough to be detected by the doctor or the family unless audiometric examination is done. The child often seems to respond normally to a watch tick and other kinds of noises. He hears spoken sound and responds to it, but he cannot distinguish many of its components. Treatment of the speech problem due to hearing loss should start with medical treatment of the cause if it can be treated. If it cannot be treated medically, the child may need amplification, auditory training, and lip-reading.

Tonsils and Adenoids.—Enlarged tonsils and adenoids rarely cause speech problems. Occasionally there will be a temporary denasal quality brought about by excessively enlarged adenoids. This usually will disappear as the adenoid mass becomes smaller. Removal of tonsils and adenoids rarely helps to eliminate a speech problem. The critical aspect with respect to infected tonsils and adenoids is the possible damage to hearing. Removal should be considered on the basis of this possibility and the effect on general health rather than as a procedure to improve a child's faulty speech.

"Tonguetie."—Parents almost universally think a child is "tonguetied" when they find a speech problem of any kind. While it is true that a very short lingual frenulum can interfere with the formation of some consonants and clarity of articulation in connected speech, this condition is rarely the only cause of a serious speech disorder. When the child has trouble with articulation and is also found to have a short lingual frenulum, his speech generally can be improved more rapidly if the frenulum is clipped. A speech pathologist generally can tell, by phonetic analysis of the speech, how much the tongue is limited in speech by the short frenulum.

Psychological Problems.—Severe emotional trauma, rejection, overly severe discipline, extreme fear, lack of a mother figure in early years, and such factors often result in major speech problems. Stuttering is one of the results of this kind of problem. Severe sustained emotional upset in the very young child or parental deprivation often will result in marked retardation in speech and sometimes complete lack of speech long beyond the age when it should have appeared. These conditions also may result in voice and articulation disorders when speech does develop. Psychiatric treatment often is indicated before speech therapy is attempted.

Environmental Conditions.—Such environmental conditions as the child's having been abandoned and brought up in a nursery away from a mother figure may cause speech delay. A major speech deviation in a parent or an older sibling may be imitated by a younger child. Specific kinds of voice quality, faulty language structure, and deviations in pronunciation are all known to be imitated by children. Lack of motivation for speech in a home may cause a child to delay the beginnings of speech. The appearance of a new baby, displacing the next youngest child as the central figure, or displacement for some other reason, may result in the displaced child reverting to baby-talk which may become a problem if not handled properly. Treatment of problems caused by environmental conditions often involves removing causes if possible. Sometimes therapy is needed, but removal of the cause often will restore adequate speech.

A Brief Guide for Checking Speech

The doctor should be concerned about the child's speech when any one or more of the following conditions exist: 1. The child is not talking at all by age 2. 2. Speech is largely unintelligible after age 3. 3. Sounds are more than a year late in appearing, according to developmental sequence. 4. There are many omissions of initial consonants after age 3. 5. There are many substitutions of easy sounds for difficult ones after age 5. 6. The child uses mostly vowel sounds in his speech. 7. There are no sentences by age 3. 8. Word endings are consistently dropped after age 5. 9. Sentence structure is noticeably faulty at 5. 10. The child is embarrassed and disturbed by his speech at any age. 11. The child is noticeably nonfluent after age 5. 12. The child is

distorting, omitting, or substituting any sounds after age 7. 13. The voice is a monotone, extremely loud, largely inaudible, or of poor quality. 14. The pitch is not appropriate to the child's age and sex. 15. There is noticeable hypernasality or lack of nasal resonance. 16. There are unusual confusions, reversals, or telescoping in connected speech. 17. There is abnormal rhythm, rate, and inflection after age 5.

When the child will not talk for the doctor, it is risky to base an evaluation of the speech entirely upon what the parents say about it. They rarely are able to report accurately concerning this aspect of their child's behavior. Generally they will give a picture of speech behavior considerably in advance of what it actually is because they read their own interpretations into what they hear. Occasionally a parent will underestimate the child's speech. Careful, detailed questioning of the parents by the doctor is needed in any case where he does not hear the child.

Doctor's Role in Diagnosis and Treatment of Speech Problems

Since the family doctor generally is the first specialist to see the child whose family feels there is a speech problem, he is in a position to give guidance that will bring about a satisfactory solution to the problem. It is not expected that the busy doctor should make a diagnosis of the specific kind of speech disorder nor offer treatment for the disorder after it is diagnosed. Neither should the doctor dismiss the matter as not important because he is not expected to diagnose or treat it. It is possible for him to do several things which will lead toward satisfactory diagnosis and treatment, if there is a problem, or removal of the fears of the parents if there is no problem.

The doctor can determine the extent of the family's concern. Often it is true that there may not be a serious speech disorder but a family's concern and resultant interference may well lead to one if they do not receive help. In the older patient his own concern with what may or may not be a problem also is important to determine. The doctor can next determine if this is a real speech disorder that may need attention or if it is a developmental phase that can be left alone. If it is the latter, the family needs reassurance and proper explanation. If there is a speech disorder, does it appear to be organic or functional? If there is a disorder which appears to be organic, are there conditions in the medical history, or from current medical examination, that suggest a cause? Are there conditions in the family's environment or the child's behavior that suggest a cause? If there is a speech problem, the doctor should know where the parents can get an adequate diagnosis and therapy if needed. If it is indicated, the doctor can make the referral to a qualified speech pathologist for a detailed evaluation of the speech and hearing. It is at this point that the doctor's telephone call, letter, memo, or report to the speech pathologist can begin to bring about the better relationship mentioned below.

The Doctor and the Speech Pathologist

There is no great difficulty in determining that a child has a speech disorder severe enough to create a problem for him, but if the problem is to be eliminated the speech pathologist must know the kind of a disorder and as much about the causes of it as can be determined. Furthermore, the speech pathologist needs to know a great deal about the child himself to be able to determine how much of a problem this will be to the child and what his potential is for overcoming it. This being the case, information will be sought from several sources. Of special value is information which the doctor who has examined the child can give. Too often, however, these examinations have been done but results are not available to the speech pathologist at the time he makes his examination. There has been a wide gulf, in many cases, between the speech examiner and the doctor. It is true that some doctors have not made it easy for the speech specialist to approach them. Speech specialists, on the other hand, sometimes have held themselves apart from the doctor, have not made adequate use of medical information when it was available, and at times have complained that they were misunderstood by the doctors and that their work was not appreciated.

What seems to be needed is a conscious attempt to open the necessary channels of communication. One or two calls or a note from the doctor to the speech pathologist about a patient will do a great deal to open these channels, especially if the doctor voluntarily offers information which he feels may be useful. This also will help to encourage the speech pathologist to approach the doctor with information that may be useful in the over-all care of the patient. I have had the fortunate experience in my present situation of seeing communication between doctors and speech specialists develop to where there is a free and easy flow of referral and information both ways. This has been accomplished because doctors in the area were willing to share information for the common good of the patient when they were given the opportunity by speech specialists.

Because the functions of language are so easily affected by physical, mental and emotional factors, a language disorder can be evaluated and treated much more effectively if the speech pathologist has specific kinds of information from the doctor. Among other things he needs to know are (1) any prenatal, birth, or neonatal disturbances that might have caused neurological injury that could interfere with the language functions; (2) congenital malformations that might relate to speech; (3) knowledge of prolonged or serious illnesses, injuries, or other severe disturbances; (4) infections which might cause damage to the hearing mechanism; (5) results of audiometric examination as part of the evaluation of all speech disorders, even though the hearing seems normal to watch or voice test; (6) a child's general developmental pattern, that is, whether he is generally retarded in motor development, physical growth, and function or whether he is developing as he should; (7) other factors, such as malfunction of the speech organs, breathing abnormalities, and abnormal coordination of muscular movements; (8) major defects of vision or hearing; and (9) an opinion as to the child's mental development. The physician is in a good position to form an opinion as to what he thinks the child's mental level may be, although neither he nor the speech pathologist will want to accept this opinion as final until adequate psychological tests are made.

After an evaluation of the speech is made, therapy may be recommended, or it may be found that the child is not yet ready for therapy. In most cases the pathologist will be reluctant to begin active speech therapy before a child's general developmental level has reached the age of 4. The child may be deficient in certain areas but the general level should be around this age. During the time the child is developing enough maturity to profit by direct therapy, much can be done by counseling with the parents—and in some cases actually training them to do speech stimulation in the home. The doctor can help a great deal here if he is informed of what the speech pathologist recommends and if he will encourage the parents to follow through with such a program. The pathologist will nearly always recommend in such cases a reexamination in six months to a year and will continue these rechecks and counseling until such time as the child is ready for therapy or exhibits adequate speech.

If therapy is recommended, the speech pathologist will know the place where the therapy can be obtained. One of the commonest problems at this stage is that many lay persons think that speech problems can be treated on a short-term basis in the same manner as the doctor handles many problems. The parents need help in understanding that a speech disorder cannot be "cured" by prescription, by operation, or by the application of a few "speech lessons." Generally the therapy will be of long duration, sometimes extending into years. The family doctor can help by advising the parents concerning this factor and encouraging them to accept the situation and cooperate fully with the speech therapist.

The Profession of Speech and Audiology

Speech pathology as a profession has developed largely within the last two decades. Major attention in the earlier years was directed toward individuals with speech problems, but the close relationship between hearing loss and speech disorders made it inevitable that the field of audiology would assume major proportions as a specialty within the field of speech pathology. Because the profession of speech and audiology is a young profession, laymen and professional people usually are not acquainted with qualifications, functions, and availability of specialists in this field. The doctor could utilize the resources of this specialty more effectively if he knew more about it. The major aspects are discussed below.

The American Speech and Hearing Association (ASHA) is the official certifying body, in speech and hearing, at the national level. In November, 1957, the American Speech and Hearing Association listed about 4,500 members. The association has a strict code of ethics and quite adequate methods for policing its own ranks. It has no legal status, however, and no jurisdiction over nonmembers. The ASHA grants membership to individuals with a bachelor's degree and a major in speech and hearing from an accepted institution. It does not recognize a "member," however, as qualified to diagnose speech and hearing disorders or to practice speech and hearing therapy until he has qualified for one of the two certification levels. Basic certification in the ASHA indicates that the holder is qualified to practice speech and hearing therapy in most situations but should work under the supervision of one holding advanced certification. Advanced certification indicates that the holder is qualified by training and experience to diagnose and treat major speech and hearing problems and to assume clinical responsibilities without supervision. An individual may be certified at either level in either speech or hearing or both.

Generally, five terms will be used to designate people working in this field. The term "speech pathologist" usually is applied to individuals holding advanced certification and whose major concern is with pathological speech conditions and the diagnosis of such. The terms "speech therapist" and "speech correctionist" generally are used to designate individuals who do the actual therapy with speech and hearing cases after the diagnosis has been made. In many cases, however, these individuals make diagnoses also. The therapist or correctionist usually holds basic certification in the ASHA or certification from a state or public school district. The term "audiologist" generally designates the same relationship to the field of hearing as speech pathologist does to speech. The term "audiometrist" is used in many areas to designate an individual trained to give audiometric tests but not to interpret or to give therapy. None of these designations are fixed and often they are interchangeable. Many persons hold certification in both speech and hearing and many therapists, pathologists, and audiologists do both diagnosis and treatment in both areas.

A number of state departments of education certify speech and hearing therapists. In general, state requirements are roughly equivalent to those for basic certification in the ASHA. This means that most public school therapists are qualified to give therapy to the more routine kinds of speech problems, and most of them are well enough trained to know when they find a problem that they should not try to handle without help from someone with more training. Often they are not sufficiently trained or experienced to diagnose the more complicated problems.

When the doctor wishes to refer a patient for diagnosis, and therapy if it is needed, it is easy for him to check on the qualifications of the clinic or the individual to whom he is referring. If a person is practicing speech therapy in a public school system, he probably is certified by the state's Board of Education. This means that he can give help with the less severe kinds of problems; he should not be asked to make complicated diagnoses. In some situations, school districts have required persons who have inadequate training to diagnose and give therapy for all kinds of problems. Sometimes parents, school officials, and family doctors are somewhat dismayed at the results. The therapist, in this case, is not to be blamed, but his situation should be understood. Outside of the public schools it may be a little more difficult to check on qualifications, but most legitimate speech and hearing specialists will hold active (not associate) membership in the American Speech and Hearing Association and will be listed in its annual directory, which is published in the *Journal of Speech and Hearing Disorders*, as holding either basic or advanced certification. This directory is available at most college and university clinics or at the office of the Executive Secretary of the American Speech and Hearing Association, 1001 Connecticut Ave. N. W., Washington 6, D. C.

As in all professional fields, there are practitioners in speech and hearing who are not qualified and who take advantage of people's disorders for financial gain. It has been easy for these people to practice in the field of speech and hearing because there has been no legal way of restraining such practice. Quackery of this sort usually has centered around the major speech disorders, such as stuttering, and pathological problems, such as cleft palate and cerebral palsy. In the field of hearing the greatest abuse occurs in connection with audiometric testing and the selling of hearing aids. There are, however, a number of private speech and hearing specialists and individuals in private clinics practicing on an ethical and sound basis. These, almost without exception, will be found to be certified by the ASHA. The doctor would render a professional service if he checked this certification before giving support to the unqualified person by making referrals to him.

The doctor could be especially helpful to patients with hearing loss if he could counsel them to have the hearing evaluated by a trained audiologist. When a hearing aid is thought to be needed, the child should be evaluated and the most useful hearing aid fitted at a speech and hearing clinic where there is a trained audiologist who will try several kinds of hearing aids. The ASHA specifically separates the selling of hearing aids from the evaluating of hearing and fitting of hearing aids. To combine these two functions is not considered ethical. Many patients are left at the mercy of high-pressure salesmen if they are not counseled as to how best to obtain the proper hearing aid.

Any modern doctor realizes that the day is past when he can be expected to supply all the answers to questions about any complaint from his patients. He will also be aware, however, that many of his patients and patient's parents still expect this of him. If both he and the speech specialist will make an effort to open the avenues of communication and cooperation between them, it will be a step toward the sharing of at least one problem area and thus easing an unreasonably heavy burden for the doctor.

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COUNCIL ON FOODS AND NUTRITION

Report to the Council

The Council has authorized publication of the following report. This article is part of a nutrition education program which is assisted by the Nutrition Foundation, Inc.

PHILIP L. WHITE, SC.D., *Secretary.*

DIETARY TREATMENT OF ADULTS WITH DIABETES MELLITUS

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Although dietary measures for the treatment of diabetes mellitus have been used for over a century and a half, uncertainty exists in the minds of many physicians today concerning the therapeutic role of diet in diabetes. Professional uncertainty is often combined with an inability to initiate and to supervise properly a suitable diet. Experience and judgment are needed to promote the dietary habits conducive to control of diabetes within the framework of the patient's everyday life.

Prior to the availability of insulin, diabetic diets were generally high in fat and protein but restricted in carbohydrate and total calories. In more severe cases, periods of complete fasting were used to prolong a precarious existence. The early insulin era was characterized by a gradual liberalization of diet restrictions, with increasing carbohydrate intakes. Normal caloric allowances replaced the semistarvation diet of former times. At present, many physicians employ diets for diabetics that differ little in composition from those of the general nondiabetic population.

An extension of this point of view is the so-called free diet, in which a few high-carbohydrate foods are prohibited, and no attempt is made to regulate food intake. The use of such diets has been associated with a much more tolerant attitude toward glycosuria; insulin is used to abort symptoms and ketosis. Many adult patients with normal weight and moderate eating habits can be successfully managed with insulin, without strict dietary regulation. However, a large body of experience attests to the urgent need for careful dietary regulation, especially in diabetics requiring insulin for therapy.

Three arguments can be marshalled in favor of the continued importance of the diabetic diet. First, it is a valuable educational procedure that helps the patient to understand his disease and leads the way to optimal nutrition. Optimal nutrition implies not only the prevention of deficiencies of essential nutrients but the attainment of an ideal caloric balance. Second, a diabetic diet obviates the use of insulin in perhaps 30 to 40% of the diabetic population. Lastly, and most important of all, diabetic diets allow the patient receiving insulin to integrate the dietary intake of carbohydrates with the time course of the insulin preparation used and permit a closer approach to normal glycemia without undue risk of insulin shock.

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The Dietary Prescription

An understanding of the average American diet is essential before a physician can intelligently prescribe for a patient. Joslin advises physicians to inquire into their own intake of calories, carbohydrate, protein, and fat and to follow a calculated diet for a period of time. This experience will help the physician understand his patients' problems and will increase his effectiveness as a teacher. In most respects, the Recommended Dietary Allowances of the Food and Nutrition Board of the National Research Council [1] apply to the diabetic patient. There is little evidence for increased nutritional needs for the stabilized, well-controlled diabetic patient.

The caloric requirement of adults depends on many factors such as sex, age, activity, and climate.[2] Experience has taught that the caloric allowances recommended by the National Research Council are about 300 to 400 calories in excess of the needs of many urban sedentary workers. For middle-aged adult diabetics, initial caloric provision of 30 to 35 calories per kilogram of ideal body weight has proved satisfactory. This may be increased to 40 to 50 calories per kilogram in nutritionally depleted or very active young patients. It is worth remembering that mechanization has reduced the physical labor in most occupations and has reduced occupational differences in caloric requirements.

When diabetes and obesity coexist, as they frequently do, restriction of caloric intake is indicated. Weight reduction improves carbohydrate tolerance, and overt evidences of diabetes may disappear entirely. Intakes of 20 to 25 calories per kilogram of ideal weight and lower may be used for weight

reduction. As diabetic control becomes established, the initial caloric prescription should be modified in accordance with the patient's weight.

The orally administered hypoglycemic agents such as tolbutamide (Orinase) should not be used in place of adequate dietary treatment. Many obese patients who respond to tolbutamide will be adequately controlled on diet alone. Weight reduction in these patients is an important objective that may be neglected if the hypoglycemic agents are used indiscriminately.

The key defect in diabetes mellitus is an inability to utilize carbohydrates normally. Consequently, regulation of carbohydrate intake is an essential feature of the diets of diabetics. Few physicians have actually advocated a high-carbohydrate diet. Carbohydrates provide 45 to 50% of the total calories in the diet of most Americans. In diabetes, a moderate restriction of carbohydrate calories to about 40%, with the avoidance of highly concentrated sugars, appears to be reasonable. A helpful shortcut to arriving at such a carbohydrate intake is to provide as grams of carbohydrate a figure which is one-tenth of the total calories. For a 2,000 calorie diet, this would provide 200 Gm. of carbohydrate. It is preferable not to reduce the carbohydrate content below 125 Gm. on low-caloric intakes. Occasionally, a patient with mild diabetes may be spared the inconvenience of insulin injections by more stringent carbohydrate restriction achieved by greater dietary distortion. For diabetic patients not receiving insulin, the distribution of dietary carbohydrates throughout the day should be relatively uniform. Urban residents customarily eat a breakfast smaller than the other two meals. Since carbohydrate tolerance is least in the morning, this diet pattern may be retained. A bedtime feeding provides a way of distributing the carbohydrate load over a longer period and thus tends to reduce daytime hyperglycemia.

Diabetic control can often be improved, and hypoglycemia can be forestalled in insulin-treated patients by adjustments of the carbohydrate content of individual meals. The propensity of protamine zinc insulin to induce hypoglycemia in the early morning hours is a constant threat that can usually be controlled by a bedtime feeding containing 15 to 20% of the day's carbohydrate intake. At present, insulins of intermediate action have largely replaced protamine zinc insulin. These insulin preparations (globin zinc insulin, isophane insulin [NPH], and lente insulin) have similar time courses, although the action of globin insulin may be less sustained than that of the other two.

A common blood sugar pattern exhibited in the forenoon is hyperglycemia; it is followed by an abrupt fall in blood sugar that may reach hypoglycemic levels by midafternoon. More normal glycemia may be established by reducing the size of the breakfast and by adding carbohydrate to the noon meal or, preferably, as a midafternoon feeding. A bedtime feeding is often unnecessary when intermediate insulin preparations are used. When hyperglycemia persists in the morning, despite dietary manipulations, the addition of crystalline insulin to the morning dose of isophane insulin or lente insulin becomes necessary. In some patients the blood sugar is lowest before breakfast, and a bedtime feeding is then indicated, as it is when protamine zinc insulin is used. Other patients who exhibit severe nocturnal hyperglycemia have relatively normal blood sugar levels during the day. Many young diabetics have this pattern and are best regulated by two doses of intermediate insulin; 20 to 30% of the total insulin of the day is given a half hour before supper instead of the entire dose given in the morning.

Under most circumstances the potential carbohydrate synthesis from protein and fat sources can be disregarded, and these nutrients may be distributed evenly among the three meals. Protein provided in the night feeding is useful in preventing early morning hypoglycemia, because it provides a supply of potential glucose which is gradually liberated by metabolic processes. There is meager biochemical justification for supposing that a fixed fraction of amino acids (such as 0.58) enters the glucose pool. Gluconeogenesis is highly variable, and such high conversions only occur during periods of intense gluconeogenesis.

The importance of protein in the diet is generally accepted. A minimum of 1.0 Gm. of protein per kilogram of ideal body weight should be provided. Increased protein intakes are required to effect repletion after marked weight loss or prolonged periods of poor control. During pregnancy and lactation higher protein intakes are required. (Provision for growth will be discussed in a separate review.) Augmented protein intakes have also been advocated as providing an easily tolerated and slowly released source of potential carbohydrate. Providing 20% of the total calories as proteins permits restriction of carbohydrate and fat calories to 40% each. This is easily achieved in relatively low-caloric diets but may be impractical because of expense in high-caloric diets. When this is the case, 15% of the calories can be provided by protein and the remaining calories divided between carbohydrate and fat.

Many dietary surveys have indicated that fat contributes about 40% of the total calories in the average American diet.[3] Fat in the diabetic diet serves a useful purpose as the principal noncarbohydrate source of calories, and carbohydrate restriction is generally balanced by an increase in dietary fat. However, the evidence relating the incidence of atherosclerosis with the composition of the diet of different ethnic groups suggests that there may be hazards connected with improper mixtures of various fatty acids and improper ratios

of fatty acids to other nutrients or to excessive caloric intakes.[4] Recent experiments, conducted independently in several laboratories, have indicated that the nature of the fatty acids ingested may influence the serum cholesterol level and lipoprotein patterns and, by implication, the likelihood of the development of atherosclerosis.[5] The serum cholesterol level is significantly higher after the administration of saturated fatty acids than after the administration of unsaturated fatty acids. (Saturated fatty acids in the diet are derived chiefly from butter, hydrogenated vegetable oils, and the so-called hard fat of meat; unsaturated fatty acids are derived chiefly from vegetable oils.)

If an imbalance in the type of ingested fatty acid proves to be etiologically related to the disturbed lipid metabolism in atherosclerosis, this finding will be of particular importance to physicians treating patients with diabetes mellitus. It is well known that in this disease the atherosclerotic process appears at an earlier age and progresses at an accelerated rate. The use of vegetable oils with a high content of linoleic acid (corn oil or cottonseed oil) may permit the physician to employ a relatively high-fat intake, which assists in the regulation of the diabetes without promoting hypercholesteremia or distorting the serum lipoproteins. On the basis of admittedly incomplete evidence, it may be recommended that for diabetic patients without stigmata of atherosclerosis 40% of the calories be derived from fat but that unhydrogenated vegetable oil be substituted to a considerable extent for hard cooking fats. A higher intake of unsaturated fatty acids with more stringent restriction of saturated fatty acids should be considered for those patients with signs of atherosclerosis.

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Educating the Patient

The greatest difficulty in successful dietary treatment of diabetes consists in transcribing the dietary prescription into menus that are not burdensome and are easily understood by the patient. Fewer and fewer diabetic patients are being hospitalized for initial regulation, and the task of instructing the patient falls on the physician's shoulders. The advice to "stay away from starches and sweets" may lead to bizarre aberrations of diet because of the patient's limited understanding of food composition. Even when a professional dietitian is available for the initial instruction of the patient, dietary treatment will not be successful unless the physician knows what the patient should be eating and can maintain the patient's interest in diet.

A minority of experts still require their patients to weigh food portions on dietetic scales.[6] Most patients are instructed to measure their diet with the available and familiar household measures of teaspoon, tablespoon, and measuring cup. The design of most diabetic diets includes the basic provision of "protective" foods and affords variety by permitting the interchange of units of foods that predominantly contain protein, fat, or carbohydrate as sources of calories. At the present time, a majority of hospitals in this country use an exchange system proposed by a committee of representatives from the American Diabetes Association, the American Dietetic Association, and the United States Public Health Service.[7] An effort was made by this committee to reclassify and standardize food values and reduce the complexity of diabetic diets. Since their introduction in 1950, these "exchange lists" have been widely accepted. The educational booklet, "Meal Planning with Exchange Lists," has had an annual distribution of over 80,000 copies.

Depending on their nutrient content, foods have been assigned to one of six "exchange lists." Whole milk and its various concentrated and fat-free forms make up list 1, which emphasizes the high nutritional value of these products for the diabetic. The next three lists contain foods of increasing carbohydrate content. Vegetables with less than 3 Gm. of carbohydrate per serving are included in list 2 and need not be measured. Vegetables of intermediate carbohydrate content such as peas, beets, and carrots are included in list 2b. A serving of these vegetables is one-half cup and provides, on the average, 7 Gm. of carbohydrate. Servings of various fruits equivalent to 10 Gm. of carbohydrate are given in list 3. The starchy vegetables, bread, and cereal products are grouped in list 4 in servings which provide 15 Gm. of carbohydrate. These items require the most careful measuring. The major protein foods are found in list 5 and the fat exchanges in list 6.

The "exchange lists" provide the physician and the patient with a simple system for dietary regulation that is easily understood and is flexible enough for restaurant eating. Although the carbohydrate content of the various groups represents a weighted mean with a considerable individual range, the total dietary intake of carbohydrate will be between 10 and 15% of the prescribed figure. The wide variation of carbohydrate content in certain foods, due to seasoning and other factors, makes greater accuracy difficult to achieve.

The illustrated booklet, "Meal Planning with Exchange Lists," and nine complete meal plans of different carbohydrate content are available to assist the physician and the dietitian and may be obtained inexpensively from the American Dietetic Association and the American Diabetes Association. These meal plans provide 40% of the calories as carbohydrate, and the gross composition resembles the recommendations mentioned previously. An attractively packaged dietary kit has also been prepared by a major pharmaceutical company. Printed

instructions for modifying the "exchange lists" to permit sodium restriction and for bland, low-fiber diets have been prepared recently. These educational aids are a great boon to the physician instituting the dietary treatment of ambulatory patients.

Space does not permit a description and evaluation of other systems of diabetic dietary management. The "exchange lists" have been emphasized because of their more universal use and greater simplicity, but other systems have certain merits that probably warrant their continued use. In one system the carbohydrate content of a standard serving of a given food is expressed in teaspoons of sugar, a unit equivalent to 4 Gm. of glucose. The system provides a flexible means for computing the carbohydrate quota of each meal. The greater freedom of this method seems to be preferred by the patients at Washington University Clinics and Barnes Hospital.

Special Foods and Sugar Substitutes

As the content of diabetic diets has approached the content of the diet of the general public, the need for special diabetic foods has decreased. Canned and frozen fruits present the greatest problem because of the sirup in which they are prepared. Water-packed fruits, both frozen and canned, are now quite widely available and are becoming more equitable in price. Diabetic ice cream, in which sorbitol replaces sugar, has little to recommend its use. The metabolism of sorbitol follows pathways similar to glucose. There is no reason why diabetics on ample caloric diets cannot include a little ice cream in their diet, and provision is made for this in the "exchange lists." A careful scrutiny of the label of diabetic candy will usually indicate sources of potential carbohydrate. These products are also expensive and are usually inferior in taste.

The substitution of fructose for glucose and starch has been recurrently advocated. Support for this practice has been claimed in biochemical studies which indicate that insulin is not required for fructose utilization. The therapeutic gains achieved with fructose given orally are meager because of the active conversion of fructose to glucose in the intestinal mucosa and liver. The dietary use of fructose as a glucose substitute cannot be recommended.

Sugar substitutes such as saccharin and the cyclohexylsulfamates have long been used by diabetics and are without significant toxicity.[8] The contribution of sodium from sodium cyclohexylsulfate to a low-sodium diet may be significant, and the calcium salt is recommended during sodium restriction. The taste acceptance of these products is strikingly varied among diabetic patients. These agents are either added to foods by the user or incorporated by the manufacturer in dietetic foods and low-caloric carbonated beverages. With patients on liberal carbohydrate intakes, there is little justification for not permitting small measured amounts of sugar for sweetening.

Almost all diabetic patients inquire concerning either alcoholic or carbonated beverages. These items provide empty calories and often carbohydrates that complicate diabetic control. If the physician decides that the occasional use of these drinks is not harmful, the caloric content of the beverage should be deducted from the carbohydrate quota. The patient who is receiving insulin should be warned of the peculiar hazards of intemperance in diabetic individuals.

Summary

The control of dietary carbohydrate and caloric intake continues to be an important element in the treatment of patients with diabetes mellitus. The composition of such diets no longer differs greatly from the diets eaten by the nondiabetic population. The ability to distribute the daily carbohydrate intake in different ways permits the physician to overcome the deficiencies of exogenous insulin preparations. The techniques of dietary education have been greatly simplified, and educational material is now available that should improve both hospital and office treatment of this disease.

The following educational material can be purchased from the American Dietetic Association, 620 N. Michigan Ave., Chicago 11, or the American Diabetes Association, Inc., 1 E. 45th St., New York 17: "Meal Planning with Exchange Lists," "Diabetic Diet Card for Physicians," "A. D. A. Meal Plans No. 1 through 9," "Sodium-Restricted Diabetic Diet," and "Bland, Low-Fiber Diabetic Diet."

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Statement of the Council

The Council has authorized publication of the following statement.

PHILIP L. WHITE, SC.D., *Secretary.*

FATS USED AS DRUGS

Reports to the Council on Foods and Nutrition recently published in THE JOURNAL of the American Medical Association have carried such statements as:

> There is little evidence that small amounts of corn oil added to a diet of ordinary foods containing moderate amounts of animal fat will result in a lowering of the cholesterol level, and there is absolutely no evidence that it will affect the regression of atherosclerosis or lessen the likelihood of the development of coronary artery disease. . . . We should like to affirm that nutritional researches in this important area of health are most promising and we are enthusiastic about them. But, we think that such enthusiasm should be directed toward further research, to get the many answers we do not have, rather than toward suggesting changes in our accustomed diets, when we are not too sure at this time if, or how, they should be changed.[1]
>
> The hypothesis that dietary fats affect atherogenesis, however plausible and appealing, remains unproved. . . . However, patients with existent or threatening arteriosclerosis may be justifiably advised to eat higher proportions of unsaturated fats.[2]

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At approximately the same time as these and related publications appeared, several pharmaceutical manufacturers began to advertise products purporting to contain large amounts of poly-unsaturated fatty acids with or without vitamin B_6 and vitamin E. Thus, these manufacturers quickly provided preparations for the use of the physician who, after studying the subject and his patients, believes that such treatment is advisable. In this way the physician may judge for himself on the basis of published data and the opinions of experts whether he will prescribe one or another of these preparations.

It might be argued that these preparations are unnecessary, as the physician could do as well or better by simple and inexpensive manipulation of the diet. However, since this may be impractical or decided against for other cogent reasons, these pharmaceutical preparations may be a real advantage on occasion. The likelihood of harm arising from their use seems unlikely so far, although it should be emphasized that final proof of harmlessness is not at hand.

Unfortunately, the matter does not rest simply upon the availability of these pharmaceuticals. They are being promoted by campaigns which, in some instances, are excessive by implication. In spite of the fact that present evidence does not justify widespread prescription of these items, the methods of promotion tend toward, or at least tacitly hope for, larger sales. The implication is that these products in some measure will prevent or modify atherosclerosis. As noted previously, this has by no means been proved. It should be reiterated that the advertising fliers and brochures usually do not state but only imply, albeit strongly, such a therapeutic effect. For example, one manufacturer states that his product "is indicated in myocardial infarction, post-myocardial infarction, angina pectoris, individuals from families with a history of high coronary disease" and several others. Another says "to correct hypercholesterolemia, to help minimize the development of atherosclerosis in all patients, especially in male patients with precordial pain, overweight middle-aged patients of both sexes, patients with visibly tortuous superficial arteries, patients with elevated blood pressure." Effective treatment of overweight and obesity with these preparations seems unlikely as they supply nine calories per gram of fat!

There are two methods for overcoming the overzealous activity of these pharmaceutical houses. First, continued education of physicians and medical students in methods of evaluating new pharmaceuticals and in sources of factual information about them is essential. Let it be admitted that, for attractiveness, the quiet black-and-white pages of scientific and professional journals are a poor second to the color-and-design display of advertisers. Yet, perhaps the satisfying feeling of studying a subject and of correlating data oneself, instead of relying upon colorful brochures, is worth the trouble. Second, pharmaceutical manufacturers should be encouraged to reevaluate their advertising literature [3] dealing with the promotion of materials for the treatment of diseases of possible nutritional origin to ensure its accuracy and avoid unnecessary misinterpretation.

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CLEAN RIVERS AND LAKES

THE APPROACH OF summer revives longing for physical activity in the great outdoors. In people who are old enough it may also revive memories, for example, of the Great Lakes as they were 50 years ago, with seemingly endless stretches of clean sandy beach lined with oaks, birches, and pines. The clean stretches are no longer endless. The rivers, too, have changed, and it is now many decades since one could swim without concern in the Illinois River, or the lower Mississippi, or the Ohio. In some rivers, in fact, even the thought of boating becomes repellent if one begins to picture the consequences of falling into the water.

The problem of polluted rivers and lakes is, of course, not confined to the United States. Its urgency in other countries is illustrated by a recent account of the "appalling" condition of the Tyne Estuary in England.[1] The Northumbrian Angler's Federation called a public meeting at Newcastle to protest against the pollution of the river by waste from industries and untreated sewage from towns. A sample of water was exhibited that looked exactly like ink. "In 1867, it is on record that the Tyne salmon netters took 500 fish on one tide. . . . Today there is not a salmon in the river." While some proposed a preliminary survey, with scientific analyses of the water, others pointed out that an obvious step of great importance could be taken at once without help from any such survey, inasmuch as "the city of Newcastle and its neighboring sanitary authorities discharged a minimum of 11 tons of untreated sewage direct into the Tyne and its lower tributaries every day of the year" so that "sewage plants, not scientific analyses, were the simple answer." It is pointed out that, aside from the million or so of anglers whose needs for recreation are frustrated by this pollution, there are many more millions who fervently desire a "bright countryside of green leaf and clean, well-fed waters."

The ugliness of a polluted river is not just something esthetically offensive. It is the token of something pernicious that threatens human existence. The preservation of normal plant and animal life in our natural waters is not just a matter of sentiment. It is a necessity if human life is to continue as we know it.

For those reasons it is gratifying to note the systematic, constructive efforts that are being made in this country to reverse the trend of pollution and to restore American lakes and streams to something like their original state. An example illustrating the magnitude of the undertaking is furnished by the Ninth Annual Summary (1957) of the Ohio River Valley Water Sanitation Commission.[2] This is a report of an interstate crusade for clean streams, addressed to the governors of Illinois, Indiana, Kentucky, New York, Ohio, Virginia, Pennsylvania, and West Virginia. The problem before the commission is a continuing one, spurred on by the steady increase in the population of the Ohio River valley and complicated of recent years by the appearance of nuclear installations at various points. New, uncontrolled industries spring up. In 1953 there were 1,247 important industrial establishments, 323 adequately controlled; in 1957 there were 1,431 industrial establishments, 717 adequately controlled. The commission scored a substantial gain, in that the number of inadequately controlled industries was reduced. Some idea of the cost of this accomplishment is conveyed by the fact that one corporation alone reported the construction of sewage works costing some 30 million dollars. Industry will continue to be a problem, for the region of the Mahoning River, a tributary of the Ohio, is described as one of the most heavily industrialized areas in the world.

The increasing population is also significant. In 1940, 35% of 7,970,000 people were served by water purification plants; in 1957, 76% of 9,951,000. Here again the purification forces have scored a gain, but not without an effort. The calendar of the commission's proceedings during 1957 contains an instructive instance of trouble with a city whose inhabitants were unwilling, for various reasons, to treat the sewage they were discharging into the Ohio.

The efforts that have been made by various states to save their rivers from pollution could be illustrated by many examples. The federal government has provided grants to states to assist the states in

1. Is Purity Worth It? editorial, Roy. Soc. Health J. **78**: 1-2 (Jan.-Feb.) 1958.
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meeting the cost of adequate measures.[3] Local pride is an important consideration especially when a river like the Wisconsin or the Illinois lies entirely within the borders of the state; its inhabitants have nobody else to blame if the river becomes a disgrace to them. Moreover, the headwaters of rivers have become so important not only in recreation but also in flood control that any proposal to convert them into purely industrial areas must be viewed with great concern. A timely example is the current exploration for copper in the region of the Namekagon, Yellow, and Totagatic rivers in northern Wisconsin. The appearance of mines and smelteries there may prove to be as valuable to the people of Wisconsin as the development of the iron-bearing areas of Minnesota has been to the people of that state. At this stage the local authorities are in a position to bargain with the mining companies. Many hope the authorities will insist from the beginning that the companies incorporate in their fundamental planning every precaution against the spoiling of the surrounding territory. This great region of marshes and lakes supplies a steady flow to its rivers throughout the summer, and the result in the past has been quite different from the calamitous alternation between flood and drouth seen in many other parts of the country. With due planning, it should be possible not only to guard against future pollution of the air and water but also to preserve these other values of a beautiful region.

It would be a pity if Americans ever became insensitive to the romance that abides in names like Susquehanna, Delaware, Colorado, St. Croix, Hudson, Columbia, Potomac, Missouri, and Cumberland. Every step toward the restoration of America's grand streams to their original clean magnificence will be the outward token of a vast improvement in the way of life for 170 million people.

CHEMICAL TESTS FOR INTOXICATION—"IMPLIED CONSENT" LAWS

Ever since 1939, when the first statute was enacted in Indiana specifically permitting the use in evidence of the results of chemical tests for intoxication, both prosecuting attorneys and defense attorneys have been concerned with the attitude of the courts toward the constitutional issues involved. Primarily, these issues have related to problems of self-incrimination, search and seizure, and due process of law. Proponents of the use of chemical tests have been diligently seeking some method whereby a properly conceived statute could obviate the subsequent raising of these questions in court.

As early as 1942 the American Medical Association considered the possible utilization of existing state drivers licensing laws as a mechanism for obtaining the necessary consent to the performance of the test on persons suspected of driving while under the influence of alcohol. Inquiry was made into the possibility of conditioning a person's privilege to use the highways in his state upon his promise to submit to a chemical test whenever the need arose. At that time it was felt that such a law was of doubtful constitutionality. Exploration of the idea continued, however, and in 1953 the state of New York enacted an "implied consent" law.

After later amendments to satisfy constitutional objections the law provides that any person who operates a motor vehicle in the state of New York shall be deemed to have consented to a chemical test any time a police officer has reasonable grounds to suspect that he is driving in an intoxicated condition. If the driver then refuses to submit to a test his license to drive shall be revoked. The law as amended has been upheld by the highest court of the state of New York against charges of unconstitutionality.

Similar legislation has since been enacted by the state legislatures of Idaho, Kansas, and Utah.

Last November the Committee on Medicolegal Problems heard a report on "implied consent" laws from its Subcommittee on Chemical Tests for Intoxication. As a result of this report, the Committee recommended to the Board of Trustees that the American Medical Association endorse uniform state legislation patterned after the New York law. The request was approved by the Board of Trustees at its meeting in February, 1958. This places the American Medical Association alongside the American Bar Association, the National Safety Council, and the National Conference of Commissioners on Uniform State Laws in the endorsement of uniform legislation patterned after "implied consent" laws.

As has been said by Prof. Fred Inbau of Northwestern University: "The implied consent statute solution to the constitutional law problems regarding chemical tests is an eminently fair and satisfactory one, both as to the state and the accused. It will set to rest the issues of self-incrimination, search and seizure, and due process which have been raised so frequently in the past. Greater progress will then be made in the efforts of law enforcement officers to curb the menace created by the intoxicated motorist."

It is hoped that the endorsement of this type of legislation by the Association will be of help to those state legislatures which are sincerely trying to find some effective means of eliminating, or at least reducing, the high percentage of highway accidents in which alcohol plays an important part.

THE A. M. A. TEAM

One of the most frequent questions received in American Medical Association headquarters is "Since I am a member of A. M. A. by virtue of my county medical society membership, just what do I get out of my affiliation with the parent association?"

First of all, the A. M. A. should not be considered the "parent" organization. More accurately it is the offspring of the 1,915 local medical societies throughout the United States and the American territories. The immediate and obvious answer to the question, however, is that a member of the A. M. A. gains status as a reputable physician, acceptance by his professional colleagues, and recognition of the right to mingle with his colleagues, particularly in their scientific discussions, to work with them for common objectives. In other words, the A. M. A. member becomes a member of the team.

The major purpose of the A. M. A. is to help the doctor help the patient. In return for A. M. A. dues a member receives a membership card that entitles him to a great many services, some direct, many indirect. A few years ago the late Dr. Rock Sleyster, then President of the A. M. A., characterized the association headquarters as a ammunition factory where products were developed for use on the battle line. Some of these products are as tangible as a pamphlet and others, equally important, as intangible as an attitude.

The most complete evaluation and description of A. M. A. services is found in the pamphlet "A. M. A. in Action," which can be obtained from headquarters office. Here all the different bureaus and councils are described and relationships with health agencies and other national health groups are illustrated.

Through studies, research, and surveys by the divisions within the A. M. A. working essentially in the field of medical economics, the association acquires information and sometimes definitive knowledge on medical care problems throughout America. Thus the A. M. A. raises the voice of American medicine in social-medical matters to the same high level it now enjoys when American medicine speaks on scientific medical matters.

American medicine is speaking to the public through the accepted channels of public information—the radio, television, and the press. If we give our community leaders, writers, commentators, officials, and legislators, both state and national, the facts, not propaganda, then they will see for themselves what an active, dynamic medical organization really is doing to safeguard the health and lives of the American public and hence will not permit medicine to become a tool of government and the politicians.

In addition to weekly and monthly publications, the association sponsors two mammoth medical meetings annually, plus special conferences; maintains a package and periodical lending library service; conducts a physician's question-and-answer service; and prepares books and articles, such as New and Nonofficial Drugs, carrying latest monographs on drugs and treatment information.

All the above and much more is made possible only because over 90% of the practicing physicians in the United States want to belong to the same team. To be sure, not all participate in team activities all the time, but the A. M. A. is unique in that there are never any "scrubs"; all are members of the first, and only, team in American medicine.

WHY PEOPLE BOUGHT LIFE INSURANCE

A recent survey of members of 3,000 spending units sampled in a continuing study by the Survey Research Center of the University of Michigan in cooperation with the Board of Governors of the Federal Reserve System indicates that life insurance is purchased for many reasons.[1] Whereas only 12% mentioned insurance as a good method of saving, 35% gave as one reason for paying premiums the establishment of a "clean-up" fund to pay outstanding bills, debts, and funeral expenses. Provision for paying the costs of the last illness is given by life insurance salesmen as one of the major reasons for buying life insurance, and this survey of persons who had purchased life insurance and continued to pay premiums thereon verifies the appeal of this familiar sales argument.

The rapid growth of voluntary health insurance has tended to obscure this time-honored role of life insurance in defraying the costs of the last illness. More than one billion dollars a year is paid out by life insurance companies for death claims of persons aged 65 and over, the age group which experiences the highest mortality rates. The funds made available through life insurance for paying medical and hospital debts for the last illness are just as useful to the surviving members of the family as are the payments made under health insurance policies. One cannot, of course, know which illness or accident will be the last, but the last one is typically the most expensive. This survey also indicates that the proportion of persons in the age group 65 and over owning life insurance increased from 52% in 1950 to 56% in 1956.

Whereas only 18% of the spending units with incomes of $7,500 or more mentioned the provision of a "clean-up" fund as one of the basic reasons for purchasing insurance, 65% of those with earnings of less than $2,000 a year were motivated in part by the desire to provide such a fund. Moreover, it is likely that many respondents who gave "to provide for dependents" as one of the reasons for buying life insurance could have had in mind the advantage to dependents of providing for the payment of debts outstanding at the time of death.

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ORGANIZATION SECTION

STATEMENT REGARDING THE HOSPITAL SURVEY AND CONSTRUCTION ACT BEFORE A SUBCOMMITTEE OF THE HOUSE OF REPRESENTATIVES

Mr. Chairman and Members of the Committee:

I am Dr. Julian P. Price of Florence, South Carolina, a member of the Board of Trustees of the American Medical Association, on whose behalf this statement is presented. Accompanying me today are Dr. Willard A. Wright, Chairman of the Committee on Medical and Related Facilities of the Association's Council on Medical Service and Mr. Joseph Miller of the Council's staff.

When the proposed hospital survey and construction act, commonly known as the Hill-Burton Act, was heard before the 79th Congress, it was considered very carefully by the American Medical Association. As a result, the intent and purposes of the legislation received our approval, and the Association has continued to support the law since its enactment. In February, 1956, our Board of Trustees requested the Council on Medical Service to conduct a comprehensive study of the Hill-Burton program. It was our belief that a complete evaluation should be made of the operation and achievement of the program, since its establishment in 1946, in order to determine whether it had accomplished the purposes for which it was enacted and to determine whether its continuation should be recommended. This project was assigned to our Committee on Medical and Related Facilities.

In evaluating the program, numerous sources of information were used. As a result of conferences held in Washington with representatives of the Public Health Service, comprehensive statistical data were obtained. Annual Survey Reports, obtained from every state and territory, were used in an examination of the program's administration and operation. Questionnaires were sent to all state and territorial medical associations and all available related data were compiled and reviewed.

Field surveys of fourteen states, selected to give an accurate cross section, were undertaken by a team of A. M. A. staff research analysts. The states visited were: Arkansas, California, Connecticut, Georgia, Illinois, Iowa, Kentucky, Maryland, Michigan, Mississippi, Montana, New Jersey, Oregon, and Washington. Because of the original emphasis in the Hill-Burton act on aid to rural and low income areas, six rural states were visited. In the states visited, the research staff interviewed over two hundred persons representing government agencies administering the program, members of state hospital advisory councils, individuals in the field of hospital administration, project sponsors, and members of the medical profession.

With your permission, Mr. Chairman, I would now like to ask Dr. Wright to discuss the results of his Committee's study and the recommendations of the American Medical Association resulting therefrom.

STATEMENT BY WILLARD A. WRIGHT, M.D., ON HILL-BURTON PROGRAM

Mr. Chairman, and Members of the Committee:

I am Dr. Willard A. Wright, Williston, North Dakota, Chairman of the Committee on Medical and Related Facilities of the American Medical Association. As Dr. Price has told you, our committee has recently completed a two-year study of the Hill-Burton program. I would like to discuss the recommendations of the American Medical Association from this study.

It is our recommendation that the Hill-Burton program be continued, although we believe that some of its objectives should be re-defined and that several changes should be made in the program in order to render it more effective. It is our conclusion that, with few exceptions, the Hill-Burton construction program has been administered efficiently and in the interests of the public, and that the objectives of the original legislation are, to a large degree, being achieved.

Emphasis now needs to be directed toward construction of facilities for the chronically ill as a part of a general hospital, toward construction of nursing home facilities, and toward the modernization, renovation and remodeling of existing hospitals. To provide this emphasis, it will in our opinion be necessary to give the states greater latitude in establishing priorities and in allocating funds.

Since its inception, one of the objectives of the program has been to give "specific consideration to hospitals serving rural communities and areas with relatively small financial resources." We have found that, for the most part, this objective has been achieved. Of the seventeen states described in the 1950 census as being fifty per cent or more rural, our staff members visited six. These six states had two hundred and thirty-five areas designated as rural. In one hundred and forty of these areas at least seventy-five percent of their hospital bed

needs had been met; fifty areas had met fifty to seventy-four percent of their needs, and only forty-five areas had met less than fifty percent of their bed needs. In these six states, we found that from sixty-two to ninety-two percent of the total federal determination for hospital beds had been met. We also found that in these states the percentage of construction funds allocated to rural areas was showing a definite downward trend. A similar downward trend in allocations for construction in rural areas was also found in the other eight rural states visited.

Therefore, we believe it is logical to assume that in most states, the special need for rural hospitals no longer exists. This was also, generally, the opinion of those persons responsible for the administration of the program in the states visited, and it is substantiated by occupancy statistics. It appears therefore that in a number of states the greatest need for hospital beds is in the metropolitan areas. Existing priority factors, however, have limited such construction. Therefore, it is recommended that mandatory priority for rural areas be abandoned and that the individual states be permitted to establish priorities in accordance with their particular needs.

In order to grant the states greater freedom in allocating funds, we would recommend that all present categorical grants, as set forth in Section 651 of the Act, be eliminated. We would substitute for these categorical grants one single appropriation for all facilities covered under the act, thus allowing maximum freedom of re-allocation.

We have found that federal assignment of specific funds to special projects, such as chronic disease facilities, diagnostic or treatment centers, rehabilitation facilities, and nursing homes, has seriously handicapped worthwhile programs in some of the states. For example, in the case of rehabilitation facilities, rigid assignments have forced some states to lose their allotment to other states. Federal assignment of funds to special-type projects also tends to increase administrative problems because of the built-in inflexibilities.

We would next recommend that the diagnostic or treatment center facility be eliminated entirely from the act. We found much confusion in the states as to what the term diagnostic or treatment centers means. There is little evidence of a need or demand for such a provision to build the ill-defined units. We believe that increases in diagnostic and treatment services for the people are dependent primarily on the availability of medical and para-medical personnel.

When it was proposed to add the diagnostic and treatment center category to the Hill-Burton program, we expressed our doubts concerning the needs of federal grants for such facilities. We also felt that the definition given in the act was vague and ambiguous. Our study has confirmed our doubts with respect to this part of the program.

We would also recommend that the public health center, as a facility, be eliminated from the provisions of the act. Since most states have provided for public health center construction through appropriate local and state tax resources, it is doubtful that the continuation of this phase of the program for the benefit of a few states is justified. We found that fourteen states had 89.4% of the total number of approved public health center projects and received 76.4% of the federal funds allocated to this category. We believe that these facilities can and should be provided by the states or local communities and that federal aid is no longer needed or justified.

Several of the bills now before this committee propose the institution of a loan program under the Hill-Burton Act. The A. M. A. has taken no position on this specific proposal. It is, however, the position of the American Medical Association that a government-insured loan program of the Federal-Housing Administration-type for hospitals and nursing homes, both nonprofit and proprietary, should be approved.

In summary our recommendations are as follows:

1. That the Hill-Burton program be continued.
2. That emphasis be directed toward construction of facilities for the chronically ill as part of a general hospital, toward construction of nursing home facilities, and toward the modernization, renovation, and remodeling of existing hospitals.
3. That priority for rural areas be abandoned and that individual states be permitted to establish priorities in accordance with their particular needs.
4. That categorical grants be eliminated in order to allow the states maximum freedom in their allocations.
5. That the diagnostic or treatment center facilities be eliminated entirely.
6. That the public health center facilities be eliminated entirely.

We are very much aware of experimentation and possible future changes in the effective utilization of hospital facilities. We feel that in any program for the future it will be necessary to examine closely and consider carefully the probability of radical changes in the methods of caring for people in hospitals. There is a distinct tendency to reduce the necessity for the length of stay and for certain highly specialized services available to everyone. These are other reasons why we feel the program should be made as flexible as possible.

In conclusion, I would again like to express the general support of the American Medical Association for the Hill-Burton program and reiterate our conclusion that it has been successful and efficiently administered. We believe that if our recommendations are adopted the states will have greater freedom in establishing priorities and allocating funds for the various facilities currently required.

We also believe that with the elimination of the specific categories of facilities mentioned we would have a better program and one that will be more effective in achieving the basic purposes of the act.

STATEMENT REGARDING AUTOMOBILE ACCIDENT PROBLEM, BEFORE A SUB-COMMITTEE OF THE HOUSE OF REPRESENTATIVES BY FLETCHER W. WOODWARD, M.D.

Mr. Chairman and Members of the Committee:

I am Dr. Fletcher D. Woodward of Charlottesville, Virginia, where I am engaged in the private practice of medicine and also serve on the faculty of the School of Medicine of the University of Virginia.

I am Chairman of the Committee on Medical Aspects of Automobile Injuries and Deaths of the American Medical Association and am appearing today on behalf of that Association. I would like first to express my appreciation for this opportunity to appear before you to tell you something of what the American Medical Association is trying to accomplish in the field of traffic safety and accident prevention.

The American Medical Association has been concerned with the problem of automobile injuries and deaths for many years. Actions of our House of Delegates on this subject are numerous and date back as far as 1929. In 1948, our House passed the following Resolution:

WHEREAS, The American Medical Association has in the past cooperated with the National Safety Council in its efforts to reduce the incidence of deaths and injuries from accidental causes; and

WHEREAS, The studies that have been made by the Bureau of Medical Economic Research of the American Medical Association have established the fact that fatal accidents cut off more years from the working lifetime of the American people than any one natural cause of death; and

WHEREAS, In the recent report made to the President by the administrator of the Federal Security Agency, it was stated that 40,000 deaths annually from accidents were preventable; therefore be it

RESOLVED, That the Board of Trustees be instructed to cooperate in every possible way with the National Safety Council and with every other agency, both public and private, concerned with accident prevention, to the end that research in accident prevention be further stimulated; that this excessive drain on hospital and medical facilities be lessened, and that the appalling loss of working years be reduced.

For more than 30 years our Association has had Committees actively working on the various aspects of the automobile accident problem. The present Committee was appointed by our Board of Trustees in 1955. Its members are chosen from physicians who by their interest and work were considered to be well qualified in this field.

We believe most people will agree that those who are called upon night and day to pronounce dead those persons killed on our highways, and who mend the broken bodies of those who are injured, can well be classified as interested and qualified in their efforts to prevent such carnage. Within the lifetime of most of us here, we have seen substantial gains by the medical and allied health professions in the conquest of disease and disability. Many of the diseases that were commonplace early in this century have been conquered or brought under effective control. Many diseases that were once widespread are now a rarity. However, accidental injuries and disabilities due to automobile accidents have become the number one public health problem of our time. We believe it is important, therefore, that the medical profession continue to increase its interest in the automobile accident problem until effective improvement is a reality.

As the result of our studies, we are convinced that if speed, recklessness and drunken driving are controlled, and if improvements in automobile design are provided to protect those involved in collisions, then the present appalling toll of injuries can be substantially reduced. We are further convinced that enough facts are at hand to accomplish this purpose now.

My statement will consist of a delineation of the several objectives of the American Medical Association's Committee on Medical Aspects of Automobile Injuries and Deaths, and a discussion of past, present, and planned activities in each case.

One of our most important objectives is to provide the practicing physician with technical medical information which will enable him to advise and inform his patients relative to driving limitations that may be involved in: a. Physiological states; b. Pathological conditions; c. Emotional disturbances; and d. Drugs and alcohol.

We realize that a certain percentage of accidents are undoubtedly caused directly or indirectly by medical conditions, drugs, and other related physical factors and that it should be our first duty to clean our own house. To this end we sponsored a symposium on Medical Aspects of Automobile Injuries and Deaths and presented it at the Association's Annual Meeting in June, 1956, in Chicago. These papers were published in THE JOURNAL, Jan. 26, 1957 issue, pages 225-262. Reprints are available and copies will be furnished to members of your Committee.

Our next objective is to prepare a comprehensive book to serve as a guide to physicians in determining fitness to drive as related to the medical back-

ground of the individual. When completed, this book will represent a compilation of medical data and the opinions of nationally recognized authorities in the various special fields of medical practice. With this information available, it should be possible for the individual physician to make a significant contribution to the welfare of his personal patients and the public at large.

Closely related to the need for factual information to aid the physician is the need to inform the driving public through use of proper media of the medical conditions which may affect their driving proficiency. We believe that many individuals would voluntarily discontinue or diminish radically their driving if they understood the dangerous possibilities involved in certain physical disorders and the potential effects of certain medications. In other words, if we supplement the technical information furnished the physician with a pamphlet written at the popular level and covering the more commonly encountered medical situations, the patient can have the advantage of something in print which will serve to instruct him as to whether he should or should not drive; and, if so, under what safeguards. It is contemplated that this information as well as the data for physicians will be published in THE JOURNAL of the American Medical Association.

There is little doubt that a great deal of attention must be given to the very serious question of who shall be permitted to drive an automobile and who shall be denied that privilege. We emphasize that driving should be a privilege rather than a right. Therefore, our third objective is to develop better medical standards for driver licensing, including preparation of a guide for license examiners and assistance to state agencies concerned with licensing. This will be based on the information compiled in the medical criteria mentioned earlier and will constitute our recommendations for state licensing agencies. We recommend that each state medical society have a committee on traffic safety. Such committees would be in a position to advise and assist state driver licensing bodies in the improvement of medical standards for licensing.

Another objective is to study and report on the design features of automobiles. In improvement of the design and safety equipment of automobiles rests the greatest possibility for rapid reduction in the automobile injury and death toll. If it is estimated that the average life of an automobile is ten years, it is apparent that a very considerable reduction in the severity of injuries and a marked reduction in fatalities could be accomplished in that time, if more attention were devoted to providing safety rather than to increased horsepower, streamlining, color, and chrome.

On the other hand, it will probably take a long time to engineer maximum safety into our major highways. It must also be recognized that on the secondary roads maximum safety in design may never be economically feasible. We would hesitate to forecast how long it will take to inculcate safe-driving practices, attitudes and proficiency into 75 or 100 million drivers.

The engineers and the designers of the automobile—a relative handful of men in the industry—virtually control the destinies of the American public on the highways. They are the men who decide which elements of safety design will be put into or left out of next year's new automobile.

There is presently available an ample body of research data which clearly indicates the definite values of certain safety features of automobile design, construction and equipment. Yet, these safety features are all too often made available as optional equipment at extra cost. The automobile industry can make a great contribution toward solution of this problem by consulting with physicians, anthropologists, psychologists, related biological scientists, and other scientific professions, and by giving realistic consideration to the wide range of physical characteristics of automobile drivers and riders and what happens to them in a collision.

In the past the automobile industry has made many important contributions to safety. However, in recent years, safety has generally been ignored in favor of other developments. The following suggestions have been repeatedly advanced by physicians, researchers, and safety engineers with but little success.

1. Anchorage for seat belts should be standard equipment. The public also needs education in the value of seat belts. The only evidence so far presented against seat belts is in the number of deaths in sports cars during roll-overs. This is not an argument against seat belts but against the design of such cars which do not provide roll-over bars. It should be quite simple to incorporate such a bar in the windshield and a second one back of the seat.

2. Crash padding of the dash, roof, and other areas should be provided.

3. An improved steering wheel and recessed post: perhaps a collapsible assembly—I have been told it could not be done and yet I saw a foreign car the other day that provided such steering assembly.

4. Safety door locks should be standard in all cars.

5. Removal of dangerous knobs, buttons, sharp edges, and other gadgets.

6. Seats should be securely anchored to the floor of the car and should be locked into position. They should also be high enough in the center to protect the neck in a rear-end impact and prevent neck-snap injury (also called whiplash).

7. Eliminate the deck behind the rear seat as a storage place for flying missiles or provide it with an effective retaining rail or construct it as a recessed pocket.

8. Eliminate sharp, pointed hood ornaments. These fill no functional need and are potentially lethal to pedestrians.

9. Eliminate other hazardous exterior design features such as sharp, pointed bumper ornaments.

In addition, we feel that the automobile industry should make an open-minded examination of other suggestions and adopt them where feasible. For example:

1. Shock-absorbing bumpers; if one drives his car into a brick wall at one mile per hour, he will be astounded at the shock transmitted by such an impact. One person testifying before your Committee intimated that to absorb the energy at 20 miles per hour in a 4,000-pound car, such a bumper would have to be 16 feet long. I am not an engineer, but it seems to me that engineers are ingenious enough to provide practical, energy-absorbing bumpers, especially at the front end, and possibly at the rear as well.

2. Polarized headlight lenses and an oppositely polarized windshield spot; this has been repeatedly suggested and I have yet to see any reasons presented as to why it should not be adopted. It would prevent glare at night and thereby prevent many pedestrian accidents and deaths.

3. Consideration should be given to the design of windshield and rear windows to meet standards based on optical principles.

4. Provide protective side-swipe bumpers along the sides.

5. Provide warning reflectors on the sides.

6. Remove tail lights from the realm of the artistic designer.

7. Provide a positive separation of turn signal lights from other lights.

8. Eliminate the glare-reflecting surfaces on the interior.

9. Provide accurate speedometers. Why do we have speedometer dials indicating up to 120 miles per hour? Why not an audible warning device to denote when safe speed has been passed?

10. Construct drivers' seats with better regard for the posture and visibility of persons of various heights.

11. Make chrome, clocks, radiator ornaments and other expensive gadgets optional equipment and install safety equipment as standard equipment.

As evidence of the interest in this subject by the entire medical profession and the conviction that something constructive can and should be done toward the prevention of injuries, I wish to quote a Resolution adopted by the House of Delegates of the American Medical Association at its meeting in Boston on Dec. 1, 1955:

WHEREAS, Traffic accidents in the United States claim 38,000 lives and 1,250,000 injured each year, with a probable 45% increase in vehicle mileage in the next ten years; and

WHEREAS, This death and accident toll could be materially reduced through improvement in automotive safety design and construction; and,

WHEREAS, All other modes of public transportation except automobile are already safeguarded by Federal safety standards; therefore be it

RESOLVED, That the American Medical Association, through its House of Delegates, strongly urges the President of the United States to request legislation from Congress authorizing the appointment of a national body to approve and regulate safety standards of automobile construction.

On Jan. 9, 1956, Dr. George F. Lull, Secretary and General Manager of the Association, addressed a letter to President Eisenhower in which he directed attention to the Resolution.

The next objective of our Committee is to promote the extension of emergency first aid training to as many citizens as possible. This training will be of value not only in connection with the reduction of the severity of automobile crash injuries, but also in connection with civil defense needs as well. We feel it is also desirable that all automobiles be equipped with first aid kits.

Related to first aid is another objective—to assist in the promulgation and to promote the use of standards for organized emergency services in local communities, including training of rescue squads and standardized equipment for rescue vehicles. This is a future activity in which we will work through state and county medical societies. An example of one problem in this area is the need for better selection, education and control of drivers of emergency vehicles. There are cases on record of ambulance drivers speeding and screaming through heavy traffic when carrying a corpse to a morgue.

As citizens and physicians, we recognize the importance of driving courses for all high school students. Similar courses should be provided for the public and the curriculum should meet certain basic educational requirements. We sincerely hope the day will soon come when such certificates will be required of all prospective drivers as well as for repeat traffic law violators.

We intend to invite representatives from all state medical societies to meet with us in San Francisco in June, 1958, at the time of the Annual Meeting of the American Medical Association. At that time, we plan to recommend a uniform group of objectives for the consideration of the state medical societies.

Since speed and driving under the influence of alcohol and their related offenses are intimately associated, we feel that stricter laws than any that now exist on our statute books should be provided. The public needs to be aroused to the point whereby the legislators will provide these laws and the traffic courts will administer them without fear and with complete impartiality.

Because of the indefatigable work of many safety organizations over the years, the incidence of death has been greatly reduced in spite of the tremendous increase in the number of vehicles and number of miles traveled. The present figure of 6.4 deaths for 100 million miles traveled is now nearly a static figure. In spite of this apparent success as to the incidence rate, the total number of deaths and injuries is increasing each year. Unless some of the suggestions mentioned above are followed, it seems inevitable that this number will continue to increase each year in spite of all the splendid work now being done.

RESEARCH KENNELS AT GEORGETOWN

The first in a series of projects to furnish more humane quarters for research animals will be dedicated July 1 at the Georgetown University Medical School in Washington, D. C. A volunteer committee of doctors and laymen, known as WARDS (Welfare of Animals used for Research in Drugs and Surgery), raised $20,000 toward construction of the university addition which will provide 40 inside-outside runs for dogs, isolation sections, ventilated rooms for cages, and places for preparation of food and sterilization of equipment.

Top, model research animal quarters to be dedicated July 1 at Georgetown University Medical School. *Bottom*, Father Thomas J. O'Donnell, regent of the medical school, receives WARDS donation from executive committee member, Mrs. Drew Pearson, holding Sandy, a canine heart patient. (*Washington Post* photo.)

This initial effort of WARDS will be followed by a similar project at the George Washington University Medical School, and it is hoped that other animal lovers across the country will form comparable committees to benefit research animals by providing them with adequate space for air and exercise while they are serving mankind. Federal matching funds paid remaining costs of the new building at Georgetown University.

Among organizations actively supporting WARDS are eight kennel clubs, the Alexandria Medical Society, the Medical Society of the District of Columbia, the National Society for Medical Research, dental and veterinary medical groups, several hospital boards, and a citizens' federation. Included among 100 WARDS committee members are 16 physicians, two clergymen, and three U. S. senators.

"The miracles of healing made possible by the use of research animals will multiply as greater attention is given to the health and comfort of our helpless 'stand-ins,'" said a WARDS spokesman. "Many diseases which, a few years ago, were fatal to both dogs and humans, have been conquered by research. Better cared for research dogs mean greater accuracy in scientific findings."

SUGGEST GUIDES FOR SOCIETIES SPONSORING PREPAYMENT PLANS

"Sponsorship of a voluntary prepayment medical benefit plan by a county or state medical association indicates progressive growth of the medical profession's basic position that the welfare of the patient is paramount in the physician-patient relationship." So states a report being submitted later this month to the A. M. A. House of Delegates, recommending adoption of guides for medical societies sponsoring voluntary prepayment medical benefit plans. After much study, the A. M. A. Committee on Prepayment Medical and Hospital Service early last month drafted a set of suggested guides for submission to its parent Council on Medical Service. On May 17, the Council voted approval of the draft in its essential form and offered it to the House for action.

The Council-ratified document states: "The wide acceptance of health insurance makes it mandatory that its effectiveness in meeting patient needs be subject, in all its aspects, to constant appraisal. The dynamic character of the prepayment institution, both in expansion of types of protection and enrollment increases, brings new problems as well as benefits. . . . Plans, prepayment or insurance, to finance the cost of medical care, in themselves influence the quality and quantity of medical care." These suggested guides for society-sponsored prepayment plans—the first of several guides—call for

assurances of free choice of physician, actuarial soundness, "the greatest possible scope of benefits (medical expanses of economic consequence) to the subscriber," maximum participation by medical society members, support of medical society policies, safeguards for continued high standards of medical practice, the right of societies to withdraw sponsorship for valid reasons, and proper and realistic contract provisions.

NEW FILM—HELPING HANDS FOR JULIE

A 7-year-old youngster is helping to influence students to choose a career on the health team. She is Julie Morgan, star of the new 16-mm. medical health career recruitment film produced by the American Medical Association, the American Hospital Association, and E. R. Squibb & Sons. "Helping Hands for Julie" tells the story of the fight to save Julie's life. The helping hands aiding the doctors in finding the correct diagnosis of meningitis are those of the nurse, medical technologists, x-ray technicians, and medical record librarians. The drugs of the pharmacist, the nourishing food of the dietician, the restorative work of the physical therapist, and the care of the nurses help bring Julie back to health.

Medical societies and auxiliaries may arrange for bookings of this 30-min., black and white sound film through the A. M. A. Film Library after July 1.

A. M. A. TO ENTERTAIN DELEGATES FROM WHO

The American Medical Association will join with four other national groups to entertain delegates to the World Health Assembly after the Assembly's meeting in Minneapolis May 26-June 14. En route home, some 250 physicians, health workers, and medical administrators from 88 countries will travel to Chicago for a two-day stopover.

The A. M. A., together with the American Hospital Association, the American College of Surgeons, the American Dental Association, and the Joint Commission on Accreditation of Hospitals, has scheduled a reception for the delegates Sunday evening, June 15. Among guests, in addition to representatives of the dental, medical, and hospital groups, will be Chicago Mayor Richard Daley and members of the Chicago consular corps. On Monday, June 16, the WHO delegates will take tours according to their special interests. One group will visit A. M. A. headquarters to learn the workings of the organization and meet members of the staff.

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

POSTGRADUATE COURSES

Notice of the following postgraduate courses has not previously been published by the Council and is presented for information only:

A five-and-one-half-day continuous intensive postgraduate course in **Radioisotopes** will be held at the University of Texas Southwestern Medical School, 5323 Harry Hines Blvd., Dallas 19, June 16-21, 1958, in association with the University of Texas Postgraduate School of Medicine. Registration for this course will be $100, and enrollment will be limited to eight registrants. Educational methods include lectures, laboratory work and demonstrations, patient demonstration, and clinical conference. Application or inquiry should be addressed to the Division of Postgraduate Education of the University of Texas Southwestern Medical School.

A three-day postgraduate course on **Dermatology** will be offered at the University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20, July 10-12, 1958, primarily for the physician in general practice. Educational methods will include lectures, demonstrations including patients, discussion, and question periods. Inquiries or applications should be addressed to the Office of Postgraduate Medical Education of the University of Colorado Medical Center at the above address.

A postgraduate course for industrial physicians and specialists in otolaryngology will be the **Institute on Industrial Deafness** at Colby College, Waterville, Maine, Aug. 10-19, 1958. The eight-day, 50-hour course will have a registration fee of $250 with enrollment limited to 30 persons. Inquiry or application should be addressed to Colby College at the above address.

The University of Puerto Rico School of Medicine, San Juan, will present a nine-month continuous intensive basic science course, for physicians in general practice, on the **Clinical and Research Utilization of Isotopes,** beginning Aug. 15, 1958. The maximum enrollment will be limited to three, at no fee. Educational methods will include laboratory work, patient demonstration, live clinic, bedside rounds, clinical conferences, seminar, lecture, panel discussion, open-question periods, and audiovisual aids, with the registrants having the opportunity of performing procedures. Further information should be obtained from the University of Puerto Rico School of Medicine.

MEDICAL NEWS

ARKANSAS

State Medical Election.—The following have been named as officers of the Arkansas Medical Society for 1958-1959: president, Dr. Louis K. Hundley, Pine Bluff; president-elect, Dr. James M. Kolb, Clarksville; first vice-president, Dr. Columbus R. Ellis, Malvern; second vice-president, Dr. Robert H. Atkinson, Hot Springs; third vice-president, Dr. John P. Ledbetter, Jonesboro; secretary, Dr. Horace E. Shuffield, Little Rock; secretary emeritus, Dr. William R. Brooksher, Fort Smith; and treasurer, Dr. Sam G. Jameson, El Dorado.

CALIFORNIA

Dr. Alway Appointed Dean at Stanford.—The appointment of Dr. Robert H. Alway as dean of Stanford University School of Medicine has been announced. Dr. Alway has been acting dean for the past year. Immediate problems confronting the new dean concern the completion of new Medical School facilities on Stanford University's Palo Alto campus. These will be contained in the now-building 22 million dollar Stanford Medical Center, scheduled for completion by the fall of 1959. Dean Alway joined the Stanford medical faculty in 1949 after teaching six years at the University of Utah Medical School, Salt Lake City. In 1953 he went to the University of Colorado Medical School, Denver, as head of pediatrics, but returned in 1955 to head Stanford's pediatrics department.

Dedicate Research Facilities at Palo Alto.—The first completed unit of the developing Palo Alto–Stanford Medical Center was dedicated May 17 by the Palo Alto Medical Research Foundation. Medical symposiums on hematology and tissue transplantation were held in connection with dedication ceremonies. The new building, costing $600,000, which was made possible by a grant from the Research Facilities Grants Division of the U. S. Public Health Service and matching gifts from private donors, consists of 30 laboratories, a library, and administrative offices. A 50-car parking area is at the rear. The Palo Alto Medical Research Foundation, established in 1947 by members of the Palo Alto Medical Clinic, is an independent, nonprofit institution affording facilities for fundamental and clinic research to doctors wishing to undertake special investigations suggested by their practice. Members of the foundation's board include Dr. Russel V. A. Lee, as president, and Dr. Marcus A. Krupp, as director.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

CONNECTICUT

University News.—Dr. Milton J. E. Senn, Sterling Professor of Pediatrics and Psychiatry, Yale School of Medicine, New Haven, has gone to Soviet Russia to study child care and rearing practices in that country. In return, a Russian doctor, as yet unknown, will come to the Yale School of Medicine late this year as a guest of the Child Study Center. ——"A New Look at Pulmonary Pathology Studies Based on Histological Sections of Whole Lungs" was presented by Dr. Jethro Gough, professor of pathology, The Welsh National School of Medicine, Cardiff, April 14, at the Yale–New Haven Medical Center.

DISTRICT OF COLUMBIA

Dr. Goodpasture Receives Gold-headed Cane.—The American Association of Pathologists and Bacteriologists' gold-headed cane, given periodically to the member who "insofar as possible represents the highest ideals in pathology and medicine," has been awarded this year to Dr. Ernest W. Goodpasture, scientific director at Armed Forces Institute of Pathology, formerly professor of pathology and dean at Vanderbilt University Medical School, Nashville, Tenn. The gold-headed cane has been held for several years by Dr. Howard T. Karsner, formerly director of the pathology institute at Western Reserve University, Cleveland, and presently consultant to the Surgeon-General of the Navy. It was first awarded in 1919 to Dr. Harold C. Ernst, Harvard University, Boston, one of the founders of the association. Other holders were: Dr. William H. Welch, Dr. Theobald Smith, Dr. Frank B. Mallory, and Dr. James Ewing.

Society News.—At a recent meeting of the District of Columbia Society of Anesthesiologists the following officers were elected: president, Dr. William E. Bageant; vice-president and president-elect, Dr. Arch S. Russell Jr.; and secretary-treasurer, Dr. Thomas F. McDermott Jr.

MASSACHUSETTS

Mental Health "Cooperative Plan".—A pioneer mental health program is being undertaken at Massachusetts Mental Health Center in cooperation with the Boston University School of Nursing. A Day Care Program permits mental patients to leave the hospital in late afternoon and spend the night with family and friends. When individuals are first admitted to the hospital, both the patient and his family are personally greeted by a doctor, nurse, and social worker. The nurse wears her street clothes, and the nurse, doctor, social worker, patient, and relatives get to know one another through an informal coffee period designed to encourage verbal interaction and allow time for normal anxieties to recede. A nurse is assigned to each person in the ward, and when the patient is released after each day's therapy, the nurse is available for home visitations. Through joint efforts of the Mental Health Center social work supervisor and hospital chaplain, the role of rehabilitation is expanded by association of Boston University social work and theology students participating in home visits. The program eliminates excessive cost of round-the-clock hospital administration, through reduction of overhead to both the institution and the individual, and the nurse is released from management functions.

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MICHIGAN

Research Building for Life Sciences at Wayne.—Plans are underway at Wayne State University, Detroit, to build a $1,500,000 Life Sciences Research Building, with construction expected to start in August. The building, made possible by a $500,000 grant given to the university on a matching basis by the Division of Research Grants of the National Institutes of Health, will provide 36,000 square feet of space. It will house research laboratories of the chemistry and biology departments. Funds for the building were awarded under Public Law 835 and provide that, besides the university supplying matching funds, the facilities are to be used solely for research purposes for a term of 10 years. Another $500,000 will be provided by the university for additional laboratories and offices for instruction and research.

Upper Peninsula Medical Meeting.—The annual meeting of the Upper Peninsula Medical Society will be held June 20-21 in the Masonic Temple, Marquette. Dr. Duncan A. Cameron, associate professor of surgery, Wayne State University, Detroit, will present the George Curry Lecture on Trauma, June 21. The program includes 12 papers and the following out-of-state speakers: Drs. John R. Hodgson, John S. Lundy, and Richard M. Steinhilber, Rochester, Minn.; Dr. Neil W. Swinton, Boston; and Dr. Paul R. Patterson, Albany, N. Y. Panel discussions on "Cancer of the Gastrointestinal Tract" and "Trauma" and movies, "The Doctor Defendant" and "Trauma," are planned. Exhibits and a program of entertainment and tours are arranged. For information write Dr. James R. Acocks, Secretary, Upper Peninsula Medical Society, Morgan Heights, Mich.

MINNESOTA

Society News.—The following officers were elected by the Minnesota Society of Anesthesiologists to serve for 1958: president, Dr. Robert C. Knutson, St. Paul; president-elect, Dr. Joseph J. Buckley, Edina; vice-president, Dr. John A. Paulson, Rochester; and secretary-treasurer, Dr. Robert T. Patrick, Rochester.——The Minneapolis Pediatric Society has elected the following officers for 1958: Dr. John D. Tobin, president; Dr. Roger I. Lienke, vice-president; Dr. Deane A. Peterson, secretary; and Dr. Elizabeth Jerome, treasurer.

Personal.—Dr. Harry M. Weber, head, section of diagnostic roentgenology, Mayo Clinic, Rochester, gave the annual Fred Jenner Hodges lecture on radiology at the University of Michigan April 11.——Dr. William C. Harrison has been appointed director of the Minnesota Department of Health's division of local health administration, succeeding Dr. Hilbert Mark who has become health officer of Toledo, Ohio.——Dr. Oscar T. Clagett, head of a section of surgery in the Mayo Clinic, was elected to honorary membership in the Irish College of Surgeons at the Charter Day meeting of that organization in Dublin Feb. 15. He also delivered the Abraham Colles Lecture before members of the college.——Dr. Arthur M. Olsen, professor of medicine, Graduate School of the University of Minnesota, was the first visiting physician pro tem at the newly established program of the Lovelace Foundation in Albuquerque, N. M., for Visiting Physicians and Surgeons pro tem, March 5-7. The program is intended to further the opportunities for graduate medical education in bringing to practicing physicians the latest advances of fundamental and clinical medicine and surgery.

NEW JERSEY

State Medical Election.—The Medical Society of New Jersey has installed the following officers: president-elect, Dr. F. Clyde Bowers, Mendham; first vice-president, Dr. Jesse McCall, Newton; second vice-president, Dr. Ralph M. L. Buchanan, Phillipsburg; secretary, Dr. Marcus H. Greifinger, Newark; and treasurer, Dr. Rudolph C. Schretzmann, Hackensack.

NEW YORK

Student Wins Alumni Medal.—This year's winner of the Association of the Alumni medal at Albany Medical College, given each year to the senior student "whose outstanding qualities give promise of his being an ideal alumnus," is Carmine W. Terraciano, of the Bronx.

Society News.—At a recent meeting of the Central New York Roentgen Ray Society, the following officers were elected for the coming year: president, Dr. Paul A. Riemenschneider; vice-president, Dr. Baird D. Jay; and secretary-treasurer, Dr. Wilbur S. Brooks, General Hospital of Syracuse, 116 E. Castle St., Syracuse 5.

Dr. Glaser Honored.—At the annual meeting of the Rochester Academy of Medicine May 13 Dr. Jerome Glaser, clinical associate professor of pediatrics, University of Rochester School of Medicine and Dentistry, was awarded the Albert David Kaiser Medal for 1958 "for his contributions to the science of medicine in the fields of allergy and pediatrics." Dr. Glaser has practiced pediatrics and pediatric allergy in Rochester since 1929.

Institute on Community Nutrition in Syracuse.—The 12th Community Nutrition Institute presented by Syracuse University will be held in two sessions, June 16-20 and June 23-27. The institute presents a public health approach to nutrition problems for nutritionists, physicians, nurses, and other professional persons. On June 20 a community case study will be held. Other topics and participants will include the following:

Water and Electrolyte Metabolism, Dr. John H. Bland, Burlington, Vt.
Nutrition in Relation to Surgery, Dr. Robert G. Ravdin, Philadelphia.
Relationships as They Affect Health and Work, Dr. Charlotte G. Babcock, Pittsburgh.
Nutrition in Pregnancy, Dr. William M. Schmidt, Paris, France.
Nutrition of the Infant and Child—A Review of Progress, Dr. Lytt I. Gardner, Syracuse, N. Y.
Intermediary Metabolism as It Affects Mental Development, Dr. Mark D. Altschule, Belmont, Mass.
The Problem of Weight Control, Martha F. Trulson, Sc.D., Cambridge, Mass.

Problems of weight control programs will be discussed June 27. Inquiries should be addressed to Dr. Anne Bourquin, Department of Foods and Nutrition, College of Home Economics, Syracuse University, Syracuse 10, N. Y.

New York City

Program for the Chronically Ill and Aged.—The New York City homestead program for the care of the chronically ill and elderly was launched officially at the Goldwater Memorial Hospital on Welfare Island March 14. The program is a development of the Public Home Infirmary Program conducted in cooperation with the State Department of Social Welfare and the city Department of Welfare which determines the eligibility to receive public assistance. A study team under the direction of Dr. Howard A. Rusk, with financing by the New York Foundation, reported in October, 1956, that "one out of every five patients in the city's municipal general and chronic disease hospitals is there not because he needs hospital services but simply because he or she has no other place to go." The team, including Mr. David M. Heyman, president of the New York Foundation, and Dr. Morris A. Jacobs, then Deputy Commissioner of Hospitals in charge of medical affairs, recommended the establishment of homestead facilities, "utilizing existing general care and chronic disease hospitals but with special provisions for the comfort, recreational and rehabilitative needs of the patients, mostly elderly men and women." It was estimated that there were between 1,740 and 2,200 patients in the 10,000 beds surveyed who no longer required hospital care, but who could not be discharged for lack of other community resources. These patients suffered primarily from neurological conditions, cardiovascular diseases, and arthritis. The Public Home Infirmary Care Program was started at Goldwater Aug. 19, 1957, for 90 patients. Additional wards were opened and now 360 beds are being utilized. PHIC beds in the entire municipal system now total 1,864 at the Bird S. Coler Memorial Hospital and Home on Welfare Island, Farm Colony on Staten Island, Elmhurst General in Queens, and at Goldwater. Additional units will be provided at Queens General, Bellevue, the Bronx Municipal Hospital Center, and at Coney Island in Brooklyn. The Hospital Research and Educational Trust, an affiliate of the American Hospital Association, has received two grants to conduct research programs relating to the homestead program and to disseminate the findings of their studies to hospitals throughout the U. S. The first of these has been supplied by the New York Foundation, which has made a grant of $25,000 a year for the next two years. The second, conducted by the Hospital Research and Educational Trust on a grant from the Office of Vocational Rehabilitation, Department of Health, Education and Welfare, Washington, D. C., will be a five-year research project aimed at developing evaluation procedures which can be easily applied to long-term patients to determine their need for continuing hospital services. Dr. Rusk will serve as the director of both projects on behalf of the Hospital Research and Educational Trust.

NORTH CAROLINA

Dr. Gross Honored.—Paul M. Gross, Ph.D., vice-president of Duke University, Durham, and president of the Oak Ridge Institute of Nuclear Studies (Tenn.), will become an Honorary Commander of the Civil Division of the Order of the British Empire, through an appointment by Her Majesty, Queen Elizabeth. The citation will be presented to Dr. Gross by Sir Harold Caccia, British ambassador to the United States, in a ceremony in Washington, D. C., for his "outstanding services to the cause of Anglo-American friendship and understanding." Dr. Gross served from 1953 until 1956 as chairman of the Southern Regional Marshall Scholarship Committee, which awarded scholarships to southern students for study in Britain. He has been a member of the Duke faculty since 1919, and also holds the posts of dean of the university and William Howell Pegram Professor of Chemistry.

PENNSYLVANIA

Personal.—Drs. Domer S. Newill, of Connellsville, D. George Bloom, of Johnstown, and Charles B. Hollis, of Philadelphia, have been appointed to membership on the State Board of Medical Examination and Licensure by Gov. George S. Leader. Drs. Newill and Bloom were appointed to fill vacancies, whereas Dr. Hollis succeeds the late Dr. Raymond S. Leopold, of Philadelphia.—Edmond J. Farris, Ph.D., executive director of the Wistar Institute of Philadelphia, delivered the annual Albert G. Swift Lecture May 1 at the New York State University College of Medicine in Syracuse on "Advances in the Treatment of Sterility."—The Nesquehoning American Legion Auxiliary has presented a citation to Dr. Albert N. Redelin "for outstanding work in the Carbon County Tuberculosis and Public Health Society and other welfare agencies." Dr. Redelin, president of the Carbon County Tuberculosis and Public Health Society since 1951, is the clinician at the State Chest Clinic at Lansford.

WISCONSIN

Dr. Turrell Comes to Milwaukee.—Dr. Eugene S. Turrell, associate professor of psychiatry, University of Colorado School of Medicine, Denver, has been appointed medical director of the Milwaukee Sanitarium Foundation and professor of psychiatry at Marquette University School of Medicine, Milwaukee, effective July 1. Dr. Turrell will devote full time to the sanitarium and the medical school. He will be in direct charge of the medical care program at the sanitarium and will organize residency training programs in psychiatry.

HAWAII

Annual Medical Election.—The results of the May 2 election of the Hawaii Medical Association are: president, Dr. William N. Bergin, Hilo; president-elect, Dr. Toru Nishigaya, Honolulu; secretary, Dr. Raymond C. Yap, Honolulu; and treasurer, Dr. Edward F. Cushnie, Honolulu.

Society News.—The following have been elected officers of the Honolulu Pediatric Society for 1958: president, Dr. Clifford K. Kobayashi; recording secretary, Dr. Robert G. Dimler; and corresponding secretary-treasurer, Dr. Donald F. B. Char.

GENERAL

Award for Essay on Surgery of Trauma.—A prize of $400 is to be given by the American Association for the Surgery of Trauma for the best essay on clinical or laboratory research in the surgery of trauma. Manuscripts, accompanied by the curriculum vitae of the author, must be received by Dr. James K. Stack, 700 N. Michigan Ave., Chicago 11, vice-president of the association, not later than Aug. 15. Contestants must be citizens of the United States or of Canada and be in residency or postgraduate training, or in the formative years of practice or teaching. The author of the winning essay will be invited to read it at the association's annual meeting, to be held at the Drake Hotel, Chicago, Oct. 2-4. The essay will be published in the *American Journal of Surgery*.

Expand Program for Practical Nurses.—Expansion of the program of the National Association for Practical Nurse Education, agency pioneering in the development of schools or practical nursing throughout the country for the past 17 years, has been announced. More than 50,000 members of state associations of practical or vocational nurses will be affected by the doubling of NAPNE's organizational structure to include a new Division of Services to State Associations, beginning June 1. To finance its expanded program, the association has adopted a budget of $200,000 for the coming year. This was made possible through grants totaling $85,000 from various foundations.

Meeting on Tuberculosis in San Francisco.—The 1958 annual meeting of the American Academy of Tuberculosis Physicians will be held June 21 at the Hotel Whitcomb, San Francisco, with Dr. Louis M. Barber, of Stockton, Calif., president of the academy, presiding. Fifteen papers are scheduled for presentation at the two sessions. Guest speaker at the luncheon will be Dr. Robert H. Alway, dean, Stanford University School of Medicine, San Fran-

cisco, who will speak on "Physicians for the Future." Dr. Barber will present the presidential address, "Present Trends and Problems in Tuberculosis," preceding the presentation of awards at the luncheon. For information write the American Academy of Tuberculosis Physicians, P. O. Box 7011, Denver 6.

Neurologists Meet in Atlantic City.—The 83rd annual meeting of the American Neurological Association will be held June 16-18 at the Hotel Claridge, Atlantic City, N. J. Dr. Israel S. Wechsler, New York City, will give the presidential address. Forty-two papers are scheduled. Four demonstrations are planned: "Use of Focused Ultrasound in Neurological Research," "Cerebral Defects by the Technique of Transillumination," "Thalamus, Cortex and Visceral Brain in Cerebral Disorders," and "Early Treatment of Ruptured Intracranial Aneurysms." The annual dinner will be held June 17, 7:00 p. m. The American Association of Neuropathologists will hold an evening meeting at the Claridge Hotel June 15 and 16. For information write Dr. Charles Rupp Jr., 133 S. 36th St., Philadelphia 4.

Diabetes Association Meets in San Francisco.—The 18th annual meeting of the American Diabetes Association will be held June 21-22 at the Hotel Mark Hopkins, San Francisco. The program includes 22 scheduled papers. The Banting Memorial Lecture will be given June 21 by Dr. Jerome W. Conn, director, metabolism and research unit, University of Michigan Medical School, Ann Arbor, on "The Prediabetic State in Man: Definition, Interpretation and Implications." At the banquet June 21, 7:30 p. m., Dr. John A. Reed, president of the association, will present an address, the Lilly award will be presented to Dr. James B. Field, Bethesda, Md., and the Banting Medal will be presented to Dr. Conn. For information write the American Diabetes Association, Inc., 1 E. 45th St., New York 17.

Disabling Illnesses Increase in 1957.—The Metropolitan Life Insurance Company Information Service reports that the incidence of disability lasting eight days or longer was about 17% higher in 1957 than in the previous year, due largely to the wide prevalence of Asian Influenza and other respiratory disorders in the final quarter of the year. Females experienced a much greater increase in frequency of disability than did male personnel. While the rate for men was about two-fifths higher in the last quarter of 1957 than in the corresponding period of the year before, the incidence of disability among women more than doubled. For the year as a whole, the increase was less than 10% for males and about 25% for females. Respiratory diseases ranked first among causes of disability for both women and men. Accidental injuries ranked second for the women and digestive disorders second for the men.

Institute on Medical Teaching in Buffalo.—The University of Buffalo and the Association of American Medical Colleges will present a Summer Institute on Medical Teaching June 16-27 "to provide a limited number of medical instructors with an opportunity to examine in some detail the problems they face in creating effective learning experiences for their students." Included will be presentation of such topics as the appraisal of student performance in clinical and laboratory settings; the use of lecture, laboratory, conference, and other techniques; the nature of the medical student population; and the historical and philosophical background of higher education as it relates to medical education. Institute leaders will include members of the university faculty. For information write Dr. George E. Miller Jr., University of Buffalo School of Medicine, Buffalo 14, N. Y.

Dermatologists Meet in San Francisco.—The 19th annual meeting of the Society for Investigative Dermatology, will be held at The Clift, San Francisco, June 21-22. Of 33 scheduled papers the following include foreign authors:

Tissue Edema—A Stimulus of Connective Tissue Regeneration, Drs. Gustav Asboe-Hansen, Martin Ole Dyrbye, Erik Moltke, and Otto Wegelius, Connective Tissue Research Laboratory, University Institute of Medical Anatomy, Copenhagen, Denmark.

Radiosodium Clearance from the Skin in Certain Cutaneous Circulatory Disorders, Dr. Ernest A. Fairburn, Queen Elizabeth Hospital, Birmingham, England.

The presidential address, "Morphology in Medicine; A Reawakening," will be given by Dr. Walter C. Lobitz Jr., of Hanover, N. H. For information write Dr. Herman Beerman, Secretary-Treasurer, Society for Investigative Dermatology, 255 S. 17th St., Philadelphia 3.

Regional Meeting at San Francisco.—The Northern California and Nevada regional meeting of the American College of Physicians will be held June 18 at the University of California Medical Center auditorium, San Francisco. A program on Fluid and Electrolyte will be presented in the morning with Harold A. Harper, Ph.D., presiding, and a program on Renal Diseases, with Dr. Henry D. Brainerd presiding, will be held in the afternoon. Topics by invited guest speakers include:

Hyponatremic and Hypernatremic States: Osmotic Aspects of Electrolyte Metabolism, Dr. Harper.

Role of Electrolyte in Regulation of Acid Base Equilibrium

—Fundamental Principles and Clinical Application, Dr. Ralph H. Kellogg, Berkeley, Calif.

Effects of Adrenal and Pituitary Hormones on Fluid and Electrolyte Metabolism, Dr. William F. Ganong, Berkeley, Calif.

Chronic Renal Failure, Dr. James Hopper, San Francisco.

Guest speaker at the evening session will be Dr. Dwight L. Wilbur, president of the college, who will present "The Third Person in Medicine." For information write the American College of Physicians, 4200 Pine St., Philadelphia 4.

Cardiovascular Meeting in San Francisco.—The sixth scientific meeting of the International Cardiovascular Society, North American Chapter, will be held June 21 at the Marines' Memorial Theater, San Francisco. A panel discussion, "Surgical Management of Coronary Insufficiency," will be moderated by Dr. Harris B. Shumacker Jr., Indianapolis. Twenty papers are scheduled, including the following with invited guest authors:

Study of Elasticized Dacron as Arterial Prosthesis: Experimental Comparison with Other Plastics, Homologous Arteries and Autogenous Veins, Drs. W. Andrew Dale and Faustino Niguidula, Rochester, N. Y.

Effects of Exposure and Infection of Synthetic Arterial Prostheses, Drs. Robert J. Schramel and Oscar Creech Jr., New Orleans.

The presidential address, "Human Values in Medicine" will be given by Dr. Shumacker at the annual dinner to be held at the Sir Francis Drake Hotel at 6:30 p. m. For information write Dr. Henry Haimovici, Secretary, North American Chapter, International Cardiovascular Society, 105 E. 90th St., New York 28.

Gerontology Awards for Summer Fellowships.—The Inter-University Council of the Institute for Social Gerontology has awarded 36 faculty fellowships for the 1958 Summer Institute in Gerontology. The fellows have been drawn from 36 universities and colleges in 24 states representing every region of the United States. The institute, to be held in August on the campus of the University of Connecticut, will provide intensive training in gerontology, "to increase the number of university and college faculty in the psychological and social sciences prepared to offer instruction and carry on research dealing with the phenomena of aging in American society." The Institute was established last year, with headquarters at the University of Michigan, through a grant from the National Institutes of Health of the U. S. Public Health Service. Sixteen universities are cooperating in the development of its program: California, Chicago, Connecticut, Cornell, Duke, Florida, Illinois, Iowa, Michigan, Minnesota, Pennsylvania State, Pittsburgh, Purdue, Syracuse, Washington (St. Louis), and Wisconsin. Directing the program is Wilma T. Donahue, Ph.D., chairman of the division of gerontology, University of Michigan, Ann Arbor.

World Tour for Four Physicians.—Under sponsorship of the Baptist World Alliance, four physicians chosen on the basis of their "professional competence and their Christian dedication," will leave San Francisco June 27 and visit clinics and hospitals around the world before returning to New York in late September. They will confer with local medical personnel in all areas and offer their services where needed. The team includes Dr. Stanley W. Olson, dean, Baylor University College of Medicine, Houston, Texas; Dr. Robert A. Hingson Jr., professor of anesthesia, Western Reserve University, Cleveland; Dr. John G. P. Cleland, director of the Cleland Clinic, Oregon City, Ore., and Dr. Charles L. Black, a chest surgeon of Shreveport, La. The team will visit mission stations and medical centers in Hawaii, Japan, Korea, and countries of Southern Asia and the Middle East, including Jerusalem and the Gaza Strip; will attend meetings of the Baptist World Alliance Executive Committee in Ruschlikon–Zurich, Switzerland, Aug. 2-8; and will tour mission stations in Africa, including Dr. Albert Schweitzer's Lamberene Hospitals. Invitation for one or more team members to visit local areas should be sent to the Baptist World Alliance, 1628 Sixteenth St., N. W., Washington 9, D. C.

Society News.—The following officers of the **American Orthopsychiatric Association** have been installed: Dr. Stanislaus A. Szurek, of San Francisco, president; and W. Mason Mathews, Ph.D., Detroit, president-elect. Executive secretary is Marion F. Langer, Ph.D., and headquarters are at 1790 Broadway, New York City.——The following officers of the **American Psychosomatic Society** took office March 29: Drs. Milton Rosenbaum, New York City, president; and Morton F. Reiser, Washington, D. C., secretary-treasurer. The 16th annual meeting of the society will be held May 2-3, 1959, in Atlantic City.——The following officers were elected for 1958-59 by the **American Association for Cleft Palate Rehabilitation:** president, Jack Matthews, Ph.D., Pittsburgh; president-elect, Dr. Jacob J. Longacre, Cincinnati; vice-president, Samuel Pruzansky, D.D.S., Chicago; secretary-treasurer, Duane C. Spriestersbach, Ph.D., Iowa City; and editor, Ernest H. Hixon, D.D.S., Iowa City.——Dr. Isidor S. Ravdin, John Rhea Barton Professor of Surgery, University of Pennsylvania School of Medicine, Philadelphia, has been elected president of the **American Surgical Association.** Other officers include treasurer, Dr. John C. Burch, Nashville, Tenn.; secretary, Dr. William A. Altemeier, Cincin-

nati; recorder, Dr. John E. Dunphy, Boston; vice-president, Dr. John D. Stewart, Buffalo; and vice-president, Dr. Frederick G. Kergin, Toronto.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	May 17, 1958 Paralytic Type	May 17, 1958 Total Cases	May 18, 1957 Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	1	1	..
New Jersey	..	1	..
Pennsylvania	..	..	1
East North Central States			
Ohio	..	..	1
Indiana	1	1	..
Illinois	..	1	1
Michigan	..	1	4
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	..	..	1
Missouri	..	..	..
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	..	..
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	1	1	..
Virginia	..	..	..
West Virginia	1	1	..
North Carolina	..	..	1
South Carolina	..	..	..
Georgia	..	..	1
Florida	1	4	2
East South Central States			
Kentucky	1	1	..
Tennessee	..	..	1
Alabama	..	..	..
Mississippi	1	1	1
West South Central States			
Arkansas	..	..	5
Louisiana	..	..	1
Oklahoma	..	..	..
Texas	4	5	23
Mountain States			
Montana	..	1	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	1
New Mexico	..	..	1
Arizona	1	3	..
Utah	1	1	..
Nevada	..	1	..
Pacific States			
Washington	..	..	..
Oregon	..	..	..
California	1	2	14
Territories and Possessions			
Alaska	..	..	..
Hawaii	3	3	..
Puerto Rico	..	..	..
Total	17	29	59

Traumatic Surgeons Organize.—An organizational meeting of the newly formed Rocky Mountain Traumatic Surgical Association was held at Aspen, Colo., Feb. 12-16. Officers elected were: Drs. Robert R. Oden, Chicago, president; Alfred C. Buergler, Akron, Ohio, vice-president; and Charles B. Bartell, Long Beach, Calif., secretary-treasurer. It was agreed to have an annual meeting in Aspen, and the dates of the 1959 meeting are tentatively Jan. 25-29. For information write Dr. Charles B. Bartell, 1600 Orange Ave., Long Beach 13, Calif.

CANADA

Annual Medical Meeting in Halifax.—The 91st annual meeting of the Canadian Medical Association will be held June 16-20, with headquarters at the Nova Scotian Hotel, Halifax. Thirteen topics are scheduled for a clinical program in color television, June 16-18. Round-table conferences on the following topics are planned: ear, nose and throat problems in children; recent advances in anesthesia; psychiatry in general practice; recent advances in dermatological therapy; and current obstetrical problems. Papers to be presented at the general sessions are:

Evolution of Infectious Diseases in the Course of History (The Blackader Oration), Rene J. Dubos, Ph.D., New York City.
Problems in Cytodetection of Early Carcinoma of the Cervix, Dr. Malcolm B. Dockerty, Rochester, Minn.
Rheumatic Fever—Prevention and Treatment, Dr. David D. Rutstein, Boston.
Relief of Deafness by Means of the Newer Operations, Dr. William J. McNally, Montreal.
Heart Sounds, Aubrey G. Leatham, M.B., London, England.
Medical Treatment of 1000 Cases of Asthma and Rhinitis, Dr. F. S. Grégoire, Montreal.

For information write the Canadian Medical Association, 150 St. George St., Toronto 5, Ontario, Canada.

LATIN AMERICA

Grant to Argentine Medical School.—To strengthen teaching and research in the basic sciences at the Faculty of Medicine of the University of Cuyo, Argentina, The Rockefeller Foundation has made a two-year grant of $100,000 to the university. Located in Mendoza on the Andean slopes of western Argentina, and founded in 1939, the university is to be housed in a University City to be built on a 155-acre park recently donated by the federal government. The Faculty of Medicine, which ensures limited enrollment and selection of students through rigid entrance requirements, has been provided with a large hospital building on the new campus. The federal government has allocated construction funds and building materials valued at almost $400,000. In the department of physiology

studies are being carried out on the physiology of respiration and muscular exercises, on cardiovascular physiology, and on arterial hypertension. Another research program, being developed in the department of histology and embryology, includes work in histophysiology of reproduction, in spermatogenesis in mammals and other vertebrates, and on the pituitary gland. A third area of emphasis in basic research is represented by the recent creation of an Institute of Biology within the Faculty of Medicine, where investigations are being continued on the ecology of amphibia.

FOREIGN

Society for the Study of Metabolism.—At the seventh meeting of the Italian Society for the Study of Metabolism in Milan in March, papers were presented on mucopolysaccharides and mucoproteins. A symposium on the factors of protein anabolism took place on the second day. Prof. Giulio C. Dogliotti (Turin) reported on his results in the treatment of underweight subjects and patients who had protein depletion with 4-chlorotestosterone acetate. The best results were obtained in those with pituitary insufficiency, hypoadrenocorticism, and hyperthyroidism. As a result of its lack of androgenic stimulation, the new steroid reportedly may be found useful in many aspects of human pathology.

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EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Written Examination.* Various locations in the United States and Canada, June 18. *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 20, 1958. *Oral.* Philadelphia, April 23-26; San Francisco, June 18-21; Chicago, Oct. 13-16. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written,* qualifying test (Part I), January 1959. Final date for filing application is July 1, 1958. *Oral Examinations 1958* (Part II): San Francisco, June 17-21; Chicago, Oct. 17-22. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 21-23, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Cincinnati, June 13-15; Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* Peoria, Ill., June 20-21. Final date for filing application was Feb. 1. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports is July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Regular Examination in Radiology.* Washington, D. C., Dec. 8-12. Final date for filing application is July 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Oral (Part II).* Los Angeles, June 16-17; Portland, June 20-21. Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Baltimore, March 10-11. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: The fall written examination will be given in September 1958 and closing date for registration is July 1. Registration for the fall oral examination closes July 1.

AMERICAN BOARD OF UROLOGY: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles, Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

ARMY

New Director of Dependent's Medical Care.—Col. Floyd L. Wergeland, M. C., has been named executive director of the Office for Dependent's Medical Care in the surgeon general's office, succeeding Major Gen. Paul I. Robinson, M. C., who has announced his intention to retire from the Army next September.

Col. Byron L. Steger will head a new personnel and training division in the surgeon general's office, organized to provide for more efficient assignment, career planning, and training of Army medical service military personnel. Colonel Steger, who entered the Army in 1933, has served abroad in New Guinea, the Philippines, Japan, and Korea. He is a diplomate of the American Board of Preventive Medicine. Reductions in military and civilian personnel resulting from the consolidations of the two divisions will be accomplished by normal attrition, according to Major Gen. Silas B. Hays, the surgeon general.

NAVY

Summer Training in the Ensign Medical Program.—Beginning July 1, 215 undergraduate medical students holding commissions in the Navy's Ensign Medical Program and who are on vacation from medical school will commence a 60-day training period in research clerkships at 12 different naval medical research activities and clinical clerkships at 14 naval teaching hospitals located throughout continental United States.

Research clerkships provide orientation and indoctrination in medical research and afford a detailed review of the research programs conducted at the training activity. Clinical clerkship training, available to the ensign medical officer who has completed at least the second year of medical school, provides indoctrination and orientation into naval medicine; rotation through the major professional services of the naval teaching hospital; and performance of on-the-job training duties commensurate with the individual's professional attainments.

VETERANS ADMINISTRATION

More Mental Patients Are Recovering.—Figures released by the VA show that an increasing number of veterans hospitalized for severe mental illness are recovering and leaving the hospital.

VA hospitals placed 6,736 mental patients on trial visits to their home communities during the first six months of fiscal year 1958, and 13,200 during the entire fiscal year 1957. The latter figure represents a 7% increase over the 12,351 patients placed on trial visit in fiscal year 1956, a 32% increase over the 9,985 patients in fiscal year 1955, and a 73% increase over the 7,617 patients in fiscal year 1953. Most of the patients leaving the hospitals on trial visit have been treated for severe mental conditions. The average daily patient load of mentally ill veterans currently in VA hospitals is 57,423, which includes 52,456 veterans with severe mental illness and 4,967 with less severe psychiatric disorders. The VA said the increase in patients on trial visit can be attributed to changes in therapies (including introduction of tranquilizing drugs and more emphasis on individual and group psychotherapy), to an increase in open wards, and to reawakened interest in development of new habits of resocialization to prepare patients for return to community living.

Personal.—Dr. Harold J. Madsen, director, professional services, VA Hospital, Downey, Ill., has been appointed manager of the VA Hospital at Fort Lyon, Colo., succeeding Dr. Howard P. Morgan, who retired March 31, 1958. The Fort Lyon hospital is a 681-bed facility for neuropsychiatric patients. Dr. Madsen, who is certified by the American Board of Psychiatry and Neurology, entered the VA in 1941 at the Downey hospital and has served there since, except for a brief assignment to the Palo Alto, Calif., VA Hospital and a period on active duty in the Navy during World War II.

PUBLIC HEALTH SERVICE

Dr. Brodie Receives Award.—Bernard B. Brodie, Ph.D., chief, Laboratory of Chemical Pharmacology, National Heart Institute, Bethesda, Md., was awarded the Distinguished Service award of the Department of Health, Education, and Welfare by Secretary Folsom in ceremonies held April 18. Dr. Brodie was cited for his development of "a new field in medicine," chemical pharmacology. The medicinal chemist may now tell in advance from the physical characteristics of a drug, and in most instances from looking at its structure, whether a drug will be absorbed from the stomach and/or intestine, whether it will be excreted rapidly, and whether it will rapidly penetrate the brain. Dr. Brodie was cited also for his development of a number of therapeutic agents and particularly for the biochemical theory of the control mechanisms in the brain that integrate the autonomic nervous system into the primitive behavioral patterns. This latter work has stimulated research in laboratories throughout the world working to uncover a basic understanding of how the brain functions.

DEATHS

Alvis, Walter Hiram ✱ Benton, Ill.; St. Louis College of Physicians and Surgeons, 1905; member of the American Academy of General Practice; veteran of World War I; on the staff of the Franklin Hospital, where he died March 17, aged 81, of pneumonia.

Asbury, William David ✱ Terre Haute, Ind.; University of Louisville (Ky.) Medical Department, 1904; past-president of the Vigo County Medical Society, Terre Haute Academy of Medicine, and the Terre Haute Rotary Club; veteran of World War I; on the staffs of the Union Hospital and St. Anthony Hospital, where he died March 29, aged 83, of injuries received in an automobile accident.

Bennett, Frank W. ✱ McAllen, Texas; American Medical College, St. Louis, 1905; on the staff of the McAllen Municipal Hospital; died March 28, aged 83, of acute heart failure.

Blair, Robert Miller, Lebanon, Ohio; Starling–Ohio Medical College, Columbus, 1913; died March 31, aged 70, of heart disease.

Bridgman, Eveleth Wilson, Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1912; assistant professor emeritus of medicine at his alma mater; veteran of World War I; during World War II, chairman of the civilian medical examiners at the Fifth Regiment Armory induction center; an associate member of the American Medical Association; formerly associated with the U. S. Public Health Service; served on the staff as medical consultant of the U. S. Public Health Service Hospital, where he died April 3, aged 69, of bronchopneumonia and nephrosclerosis.

Burdsall, Harry Lincoln ✱ Hamilton, Ohio; Medical College of Ohio, Cincinnati, 1905; veteran of World War I; associated with Fort Hamilton Hospital and the Mercy Hospital, where he died March 5, aged 79, of coronary atheromatosis and tuberculosis of the left kidney.

Bush, Edgar Murray ✱ Hampstead, Md.; University of Maryland School of Medicine, Baltimore, 1896; for many years mayor of Hampstead; died April 3, aged 87, of arteriosclerotic cardiovascular disease.

Byrne, John McCauley ✱ Delphi, Ind.; University and Bellevue Hospital Medical College, New York City, 1941; certified by the National Board of Medical Examiners; city health officer; veteran of World War II; on the staffs of Lafayette Home Hospital and St. Elizabeth Hospital in Lafayette, where he died March 31, aged 42, of injuries received in an automobile accident.

Carberry, Francis Vincent ✱ Chicago; University of Illinois College of Medicine, Chicago, 1913; veteran of World War I; died April 15, aged 67, of arteriosclerotic heart disease.

Caserta, Pietro ✱ Morgantown, W. Va.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1923; associated with Vincent Pallotti Hospital and the Monongalia General Hospital, where he died March 17, aged 62, of cerebral thrombosis.

Chamberlain, Ben H. ✱ Alhambra, Calif.; State University of Iowa College of Medicine, Iowa City, 1903; past-president of the board of education; for many years associated with the Alhambra Community Hospital, where he was administrator and where he died March 23, aged 77.

Clark, William Irving ✱ Worcester, Mass.; born in New York City April 12, 1879; Columbia University College of Physicians and Surgeons, New York City, 1904; fellow of the American College of Surgeons; member of the American Academy of Arts and Sciences; for many years on the faculty of Harvard Medical School, Boston; served as chairman of the Harvard Advisory Committee on Prison Hygiene, a member of the President's Housing Committee, and the Committee on Costs of Medical Care; during World War I attached to the American Red Cross, serving overseas and later commissioned a captain in the medical corps of the U. S. Army; trustee of Worcester Art Museum; consultant, industrial surgery at the Memorial Hospital, where he was trustee and vice-president; consultant and retired medical director of the Norton Company, where he was associated for 47 years; joint author of "Industrial Medicine"; died in the Memorial Hospital April 5, aged 78, of bronchopneumonia and Hodgkin's disease.

Cochran, Claude Malcolm ✱ Okemah, Okla.; University of Illinois College of Medicine, Chicago, 1924; died March 18, aged 68.

Cohn, Hermann, Newark, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1901; an associate member of the American Medical Association; associated with the Presbyterian Hospital, where he died March 30, aged 86, of arteriosclerotic heart disease.

✱ Indicates Member of the American Medical Association.

Corbett, Elizabeth Louise Ufford, San Jose, Calif.; University of Kansas School of Medicine, Kansas City, Kan., 1943; specialist certified by the American Board of Pathology; an associate member of the American Medical Association; interned at the Albany (N. Y.) Hospital; served a residency in pathology at Grasslands Hospital in Valhalla, N. Y., and the Kansas Medical Center in Kansas City, Kan.; served on the staff of the San Jose Hospital; died March 23, aged 41, of leukemia.

Covert, Jay Byington, Geneva, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1902; an associate member of the American Medical Association; associated with the Geneva General Hospital; died March 25, aged 82, of arteriosclerosis and hypertension.

Crow, Will Frame, Moundsville, W. Va.; Eclectic Medical Institute, Cincinnati, 1894; veteran of World War I; formerly member of the legislature, serving as a member of the House of Delegates from Marshall County; died in Sistersville March 26, aged 92.

Cummings, Michael Penn, Reidsville, N. C.; Jefferson Medical College of Philadelphia, 1911; past-president of the Rockingham County Medical Society; for many years county coroner and city health officer; served as mayor; on the staff of the Annie Penn Memorial Hospital; died March 30, aged 71, of a heart attack.

Devere, Frederick Hewitt ✱ Cranston, R. I.; University of Vermont College of Medicine, Burlington, 1898; died in the Roger Williams General Hospital, Providence, March 29, aged 83, of pulmonary edema.

Dixon, C. Harold ✱ Fulton, Mo.; Northwestern University Medical School, Chicago, 1939; veteran of World War II; a member of the staff of State Hospital number 1; died in Boone County Hospital, Columbia, March 31, aged 46, as the result of a fall.

Donald, E. Wendell, Kansas City, Kan.; University of Oklahoma School of Medicine, Oklahoma City, 1942; member of the Kansas Medical Society and the American Academy of General Practice; veteran of World War II; formerly practiced medicine in Caldwell, where he was a member of the school board; on the staffs of the Veterans Administration Hospital in Kansas City, Mo., and the University of Kansas Medical Center; died in Prairie Village March 1, aged 43, of carcinomatosis.

Dutcher, Willis Woodford, Los Angeles; Albany (N. Y.) Medical College, 1906; died March 25, aged 80.

Fidler, Charles ✱ Milwaukee; Rush Medical College, Chicago, 1906; formerly on the faculty of the Marquette University School of Medicine; fellow of the American College of Surgeons; past-president of the State Medical Society of Wisconsin; served as secretary and president of the Medical Society of Milwaukee County; veteran of World War I; an honorary member of the staff of Milwaukee Children's Hospital; associated with Columbia Hospital and St. Mary's Hospital, where he died March 27, aged 77, of periarteritis nodosa.

Fox, Francis Harry, Las Vegas, Nev.; Jefferson Medical College of Philadelphia, 1902; died March 20, aged 77, of cerebral hemorrhage.

Frazin, Nathaniel Daniel ✱ Silver City, N. M.; Northwestern University Medical School, Chicago, 1911; died April 10, aged 68.

Gaetane, Joseph Anthony ✱ Flushing, N. Y.; Boston University School of Medicine, 1937; certified by the National Board of Medical Examiners; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; veteran of World War II; president of the Queens Gynecological Society; associated with the Queens General and Mary Immaculate hospitals in Jamaica, and the Flushing (N. Y.) Hospital, where he died April 1, aged 47, of carcinoma of the rectosigmoid.

Garrett, Frank Bernard, Rockingham, N. C.; North Carolina Medical College, Charlotte, 1912; member of the Medical Society of the State of North Carolina; died in the Duke Hospital, Durham, March 27, aged 67, of uremia.

Hamilton, E. Mendel, Belington, W. Va.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1897; an associate member of the American Medical Association; served as city health officer; died March 22, aged 86, of chronic myocarditis.

Harbaugh, Ross Wallace, San Francisco; Stanford University School of Medicine, San Francisco, 1913; an associate member of the American Medical Association; died April 2, aged 73, of injuries received in an automobile accident.

Harris, Harry Gustavus, Dayton, Ohio; New York Homeopathic Medical College and Flower Hospital, New York City, 1912; died March 25, aged 80, of arteriosclerotic heart disease.

Harshberger, Joseph Walter, Fayetteville, Pa.; Chicago College of Medicine and Surgery, 1911; veteran of World War I; died in the Philadelphia Freemason's Memorial Hospital, Elizabethtown, March 21, aged 72, of cerebral hemorrhage.

Higgins, Robert Frank ✱ Tuskegee, Ala.; University of Tennessee College of Medicine, Memphis, 1931; veteran of World War II; died in Fort Lauderdale Beach, Fla., March 27, aged 56.

Hord, Benjamin A. ✦ Richmond, Va.; Medical College of Virginia, Richmond, 1898; associated with the Stuart Circle Hospital; died March 23, aged 80, of uremia.

Illsley, Wilbur Wallace, Fullerton, Calif.; Kansas City (Mo.) University of Physicians and Surgeons, 1924; veteran of World War I; died in St. Joseph Hospital, Santa Ana, March 30, aged 67, of heart disease.

Jacobson, Clara ✦ Chicago; Rush Medical College, Chicago, 1913; member of the American Trudeau Society; for many years on the staff of the South Shore Hospital; died April 13, aged 70, of acute coronary occlusion.

Jones, Thomas Edward, Washington, D. C.; Howard University College of Medicine, Washington, 1912; formerly on the faculty of his alma mater; served in France during World War I and won the Distinguished Service Cross for gallantry in action; also held the French Croix de Guerre for extraordinary heroism in action near Binarville, France; for many years associated with the Freedman's Hospital; died April 4, aged 77, of coronary thrombosis.

Kohlenbach, Stephen ✦ Columbia, Ill.; St. Louis College of Physicians and Surgeons, 1902; died in St. Mary's Hospital, East St. Louis, March 13, aged 85.

Kraft, Adolph ✦ Chicago; University of Illinois College of Medicine, Chicago, 1922; fellow of the International College of Surgeons and the American College of Surgeons; associated with Oak Park (Ill.) Hospital, Belmont and Loretto hospitals, and St. Anne's Hospital, where he died April 15, aged 62, of acute myocardial infarction.

Kuhn, Hugh Alva Ross ✦ Hammond, Ind.; born Nov. 16, 1895; University of Cincinnati College of Medicine, 1921; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, Indiana Academy of Otolaryngology, of which he was past-president, American Laryngological, Rhinological and Otological Society, American Society of Ophthalmic and Otolaryngologic Allergy, of which he was past-president and vice-president, and the American College of Allergists, serving as regent, and in 1957 vice-president; fellow of the International College of Surgeons; secretary of the Section on Laryngology, Otology and Rhinology, American Medical Association from 1953 to 1958; member of the board of directors of the Hansel Foundation; veteran of World War I; medical superintendent of the Kuhn Clinic Hospital; consultant on the staff, South Chicago Community Hospital in Chicago; staff member of St. Margaret Hospital in Hammond, St. Catherine's Hospital, East Chicago, and Our Lady of Mercy Hospital in Dyer; in 1957 received the doctor of science degree from Muskingum College in New Concord, Ohio; died in Chicago April 17, aged 62, of coronary occlusion.

Lamberth, James Vann ✦ Pineville, La.; Louisiana State University School of Medicine, New Orleans, 1953; interned at T. E. Schumpert Memorial Sanitarium in Shreveport; later practiced in De Quincy; associated with the Central Louisiana State Hospital; died March 23, aged 37, of asphyxiation as the result of a fire in his home.

Latimer, James Brockington ✦ Lieut., U. S. Navy, retired, Anderson, S. C.; Medical College of South Carolina, Charleston, 1917; entered the U. S. Navy in 1917 and retired Sept. 19, 1921; veteran of World War I; associated with Anderson Memorial Hospital, where he died April 1, aged 66, of carcinoma of the lung with metastases.

Lawson, Henry Carnie ✦ Fall River, Mass.; Cornell University Medical College, New York City, 1932; certified by the National Board of Medical Examiners; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; consultant, St. Anne's Hospital; chief of obstetrics and gynecology service, Union Hospital, where he died March 25, aged 51, of acute myocardial infarction and hypertension.

Levin, Harris ✦ Senior Surgeon, U. S. Public Health Service Reserve, Philadelphia; Temple University School of Medicine, Philadelphia, 1947; service member of the American Medical Association; specialist certified by the American Board of Pediatrics; veteran of the Korean War; associated with the Graduate Hospital of the University of Pennsylvania and Albert Einstein Medical Center, Northern Division; certified by the National Board of Medical Examiners; died April 8, aged 35.

Lewis, George Willard, Pierpont, Ohio; Western Pennsylvania Medical College, Pittsburgh, 1895; veteran of World War I; associated with the Brown Memorial Hospital in Conneaut, where he died March 25, aged 87.

Little, Edwin Gray ✦ Gadsden, Ala.; Birmingham Medical College, 1905; associated with Holy Name of Jesus Hospital and Baptist Memorial Hospital; died March 23, aged 78, of bronchopneumonia.

McClure, Daniel Vincent, Buffalo; Niagara University Medical Department, Buffalo, 1894; past-president of the Medical Society of the County of Erie; died March 6, aged 84.

McCreery, Albert Hill, Chapel Hill, N. C.; University of Pittsburgh School of Medicine, 1913; an associate member of the American Medical Asso-

ciation; formerly practiced medicine in Pittsburgh, where he was associated with the Shadyside Hospital; died in the North Carolina Memorial Hospital March 23, aged 67.

McDonald, John ✦ San Francisco; College of Physicians and Surgeons of San Francisco, 1921; veteran of World War I; died in Crawfordsville, Ind., March 28, aged 66.

McDonald, Robert Clarence ✦ Brigadier General, U. S. Army, retired, Washington, D. C.; born in Bells, Tenn., Feb. 18, 1881; Tulane University School of Medicine, New Orleans, 1909; service member of the American Medical Association; fellow of the American College of Surgeons; entered the medical corps of the regular Army in February, 1911; saw duty on the Mexican Border; served in France during World War I; awarded the Legion of Merit for exceptionally meritorious conduct in the performance of outstanding services as surgeon, Fourth Service Command; retired Feb. 28, 1945; died in the Walter Reed Army Hospital March 17, aged 76, of arteriosclerotic heart disease.

McDowell, Orrin Clark ✦ Orrville, Ohio; Ohio State University College of Medicine, Columbus, 1917; veteran of World War I; died March 28, aged 64, of cerebral embolism and bacterial endocarditis.

Makowski, Stanley Joseph ✦ Glen Cove, N. Y.; Rush Medical College, Chicago, 1931; certified by the National Board of Medical Examiners; fellow of the International College of Surgeons and the American College of Surgeons; associated with Meadow Brook Hospital in Hempstead, St. Charles Hospital in Port Jefferson, and the Community Hospital, where he died April 4, aged 54, of cerebral thrombosis.

Miller, James Preston, DeLand, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; University of Nashville (Tenn.) Medical Department, 1900; died March 10, aged 82.

Morrow, Frank M., Leavenworth, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1905; died in the University of Kansas Medical Center, Kansas City, March 13, aged 78, of a cerebral vascular accident.

Neef, Frederick Emil, Middlebury, Vt.; born July 11, 1872; Columbia University College of Physicians and Surgeons, New York City, 1904; fellow of the American College of Surgeons; formerly practiced medicine in New York City, where he was on the faculty of the Fordham University School of Medicine, and on the staffs of Lincoln, St. Elizabeth's, St. Francis, Lenox Hill and Misericordia hospitals; served on the staff of the Rockaway Beach (N. Y.) Hospital; author of a textbook of "Surgical Nursing"; died in the Porter Memorial Hospital March 24, aged 85, of arteriosclerosis.

O'Connell, Thomas Andrew, Brookline, Mass.; College of Physicians and Surgeons, Boston, 1937; died March 11, aged 61.

O'Hara, John Gerald ✦ Woodland, Calif.; St. Louis University School of Medicine, 1936; member of the American Academy of General Practice; past-president of the Yolo County Medical Society; major in the medical corps of the U. S. Army from 1953 to 1955, serving in Korea and Japan; served as part-time health officer of Yolo County; associated with the Mercy and Sutter hospitals in Sacramento, and Yolo General Hospital; died March 20, aged 46, of lung cancer.

Polk, Joseph Feaston, Slidell, La.; Memphis (Tenn.) Medical College, 1900; died March 22, aged 82.

Powell, Robert Joshua ✦ Atlantic City, N. J.; Howard University College of Medicine, Washington, D. C., 1914; past-president of the Medical Society of New Jersey; died March 24, aged 71, of cerebral embolism.

Power, George Aloysius, Worcester, Mass.; Harvard Medical School, Boston, 1909; member of the Massachusetts Medical Society; served as city physician and as a member of the board of education; died in St. Vincent Hospital March 22, aged 74, of arteriosclerotic heart disease.

Rogers, Henry William, San Rafael, Calif.; University and Bellevue Hospital Medical College, New York City, 1919; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War I; served as chief psychiatrist at the California State Prison in San Quentin; chief psychiatrist at the Department of Corrections Reception Guidance Center in Vacaville; died in the San Rafael General Hospital March 28, aged 66, of cerebral hemorrhage.

Roth, Julius Andrew ✦ Delray Beach, Fla.; St. Louis University School of Medicine, 1930; veteran of World War II; associated with Good Samaritan and St. Mary's hospitals in West Palm Beach; chief of obstetrics and gynecology at Bethesda Hospital; died March 19, aged 51, of coronary thrombosis.

Schell, Charles Peter ✦ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; member of the American Academy of General Practice; served on the staff of St. Mary of Nazareth Hospital; died April 10, aged 85, of a cerebral vascular accident.

Schneller, Edwin Jacob ✦ Racine, Wis.; Rush Medical College, Chicago, 1925; member of the American Academy of General Practice; past-president of

the Racine County Medical Society; veteran of World War I; associated with St. Luke's Hospital, where he died March 27, aged 64, of acute coronary thrombosis.

Schroeder, Frank Nicholas ✦ Ryan, Iowa; St. Louis College of Physicians and Surgeons, 1905; died in the Mercy Hospital, Cedar Rapids, March 24, aged 80, of coronary occlusion.

Scifres, Zach McNorman, Louisville, Ky.; Indiana University School of Medicine, Indianapolis, 1915; died in the Norton Memorial Infirmary March 8, aged 77.

Shaw, Francis Clark, Dannemora, N. Y.; University of Vermont College of Medicine, Burlington, 1920; member of the American Psychiatric Association; director of the Dannemora State Hospital; served on the staffs of Matteawan State Hospital in Beacon, and Lawrence State Hospital in Ogdensburg; died in the Montreal General Hospital, Montreal, Que., Canada, April 6, aged 61.

Slanec, Charles George ✦ Chicago; Chicago Medical School, 1922; veteran of World War I; died April 10, aged 66, of acute coronary occlusion.

Slopanskey, Frank Robert, Salt Lake City; Denver and Gross College of Medicine, 1905; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; formerly practiced medicine in Helper, Utah, where he was mayor, and vice-president of the Helper State Bank; a staff member of St. Mark's Hospital; died March 29, aged 78.

Stanard, Delbert Coshow ✦ Eugene, Ore.; University of Oregon Medical School, Portland, 1921; past-president of the Lane County Medical Society; veteran of World Wars I and II; died in the Sacred Heart General Hospital March 27, aged 67, of cirrhosis of the liver.

Stark, Leander William, Long Beach, Calif.; College of Physicians and Surgeons, Los Angeles, 1919; an associate member of the American Medical Association; died March 25, aged 66, of acute coronary thrombosis.

Suwalsky, Adelbert L. ✦ Leavenworth, Kan.; Medico-Chirurgical College of Kansas City, Mo., 1901; served as city physician and county health officer; associated with Cushing Memorial Hospital and St. John's Hospital, where he died March 27, aged 78, of gangrenous cholecystitis, coronary sclerosis, and pulmonary edema.

Tran, Irving ✦ Brooklyn; Cornell University Medical College, New York City, 1909; fellow of the American College of Surgeons; associated with the Jewish Hospital; died April 3, aged 70, of a heart attack.

Vest, Samuel Alexander Jr., Charlottesville, Va.; born in Haw River, N. C., Jan. 21, 1905; Johns Hopkins University School of Medicine, Baltimore, 1930; specialist certified by the American Board of Urology; professor and chairman of the department of urology at the University of Virginia Department of Medicine; formerly associate in urology at Johns Hopkins University School of Medicine and on the staff of the Johns Hopkins Hospital in Baltimore; served as vice-president of the Virginia Urological Society; member of the American Association of Genito-Urinary Surgeons and the American Urological Association; fellow of the American College of Surgeons; on the staff of the University of Virginia Hospital, where he died April 6, aged 53, of acute myocardial infarction.

Webb, Lewis Monson ✦ St. Louis; St. Louis University School of Medicine, 1925; associated with Deaconess and Bethesda hospitals; died in Fort Lauderdale, Fla., April 2, aged 61, of coronary occlusion.

Weinstein, Samuel ✦ Richmond, Va.; Medical College of Virginia, Richmond, 1925; veteran of World War I; associated with the Stuart Circle Hospital and the Retreat for the Sick; died April 3, aged 61, of coronary thrombosis.

Weir, Claud Hill ✦ Seattle; Columbia University College of Physicians and Surgeons, New York City, 1904; specialist certified by the American Board of Otolaryngology; died in the Fairfax Sanitarium in Juanita March 8, aged 80, of carcinoma of the prostate.

Whitacre, Floyd Stanley ✦ San Antonio, Texas; St. Louis College of Physicians and Surgeons, 1909; for many years a director of the Abilene (Texas) Christian College; died March 25, aged 75, of basilar cerebral artery syndrome, arteriosclerosis, and Laennec's hepatic cirrhosis.

Whitmire, William Lincoln ✦ Sumner, Iowa; Rush Medical College, Chicago, 1890; died in the Community Memorial Hospital March 25, aged 93, of arteriosclerosis.

Wilson, Franklin Samuel ✦ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; assistant professor of medicine emeritus at his alma mater; past-president of the University of Illinois Alumni Association; for many years medical examiner for the Juvenile Home; served with the Cook County Public Welfare Department; associated with the Garfield Park Community Hospital, where he died April 10, aged 85, of carcinoma of the prostate with metastasis.

FOREIGN LETTERS

AUSTRIA

Deafness in Children.—At the meeting of the Society of Physicians in Vienna on April 11, Dr. G. Koenig said that all children who do not react to sound, do not copy speech, or do not speak articulately from the time they are 2 years old should be examined to find the cause. A fairly accurate audiogram can be made for children age 2, but better results are obtained after they reach the age of 3. If a hearing defect is discovered the child should be placed in a special kindergarten where articulation exercises are started. Later systematic hearing training is practiced. As soon as the child reacts to hearing impressions, a hearing aid is provided. The child soon learns to handle the apparatus under proper guidance, but the true value of the hearing aid to the child can be determined only after 6 months of use. Even in children with no residual hearing but with normal intelligence a primitive phonetic communication may be achieved.

Blockage of Ovulation.—At the same meeting Drs. G. Schubert and F. X. Wohlzogen said that ovarian follicles just before they burst contain a substance which splits up the mucopolysaccharides of the liquor folliculi. This splitting and the resultant increase of the osmotic pressure is the eliciting cause of ovulation. Hyaluronidase splits mucopolysaccharides of the hyaluronic acid and chondroitic sulfonic acid type, both of which occur in the follicle. It was therefore important to find out whether hyaluronidase blocking agents would also inhibit the splitting of the mucopolysaccharides in the ovarian follicle, thus blocking ovulation. Adult rabbits were given 250 international units of chorionic gonadotropin intravenously to elicit ovulation. Germanin was given intravenously as a hyaluronidase blocking agent, partly simultaneously and partly after the injection of chorionic gonadotropin. The ovaries were removed 15, 24, and 48 hours after the administration of the gonadotropin and were examined macroscopically and histologically. Pretreatment with Germanin alone had no effect on ovulation, but when Germanin was given in such a way that a high level was present at the time of the expected ovulation, the latter was blocked. Thus blocking of ovulation was achieved in a different way than by blocking of the luteinizing hormone of the anterior lobe of the hypophysis by progesterone or inactivation of gonadotropin by antihormones or vegetable extracts. It is essential that neither the gonadotropic function of the anterior lobe of hypophysis nor the hormonal function of the ovary be impaired by the blocking agent.

Liver Biopsy.—At the meeting of the Society of Physicians in Vienna on April 18, Dr. Thaler reported on a new method of liver biopsy that shows one definite advantage over the method previously used, namely that of being performed without the stylet. A series of 170 such biopsies have been performed without any untoward effects. The results were excellent. Complaints after puncture were rare and usually insignificant. Thus the new technique seems to be the method of choice for needle biopsies.

Subdural Hematoma.—At the same meeting Drs. H. Reisner and E. Scherzer reported on 17 patients with subdural hematoma who were referred to the apoplexy ward of a mental hospital with a diagnosis of cerebral accident. Of the 16 patients who were operated on, 13 were cured and 3 died. It was pointed out that subdural hematoma may be present in patients with a diagnosis of cerebral accident in whom neurological symptoms are progressive. In such patients cerebral angiography should be performed.

BRAZIL

Congress of History of Medicine.—At Rio de Janeiro in April under the honorary chairmanship of Dr. Juscelino Kubitschek, President of Brazil and the only chief of state of the Americas who is a physician, the First Pan American Congress of History of Medicine and the third annual meeting of the Brazilian Institute of Medicine was held. The occasion was used to found the Pan American Academy of History of Medicine and to inaugurate, at the National Library, a bibliographic exposition of history of medicine.

Control of Trachoma.—The Ministry of Health issued a report on the campaign begun in 1957 to eradicate trachoma, which, according to the best estimates, afflicts about a million people, or 1.6% of the total population, mostly in rural areas. The work, performed by teams of physicians and nurses of the Division of Rural Hygiene began in two counties in the state of Ceará, where more than 30,000 patients were cured last year. To avoid personal contact between trachomatous patients and healthy persons, the treatment was brought

The items in these letters are contributed by regular correspondents in the various foreign countries.

to the patient's home. A total of 125,000 houses were visited, and 230,000 persons were treated, for whom 12 million sulfonamide tablets and 363,000 tubes of antibiotics were furnished. The eradication of the disease is expected to be completed within a few years.

The Spermogram.—The idea that azoospermia is the only factor to be considered for the diagnosis of sterility in men has been abandoned, and a complete study, macroscopic and microscopic, of the semen is now deemed necessary. Dr. M. L. Antunes (*O Hospital* **53**:383, 1958) reported the results of the examination of the semen of 100 husbands of pregnant women. The volume of the ejaculate varied between 1.5 and 7 cc. (average 3.1). The number of spermatozoa per cubic centimeter varied between 12 million and 214 million (average 80 million). The total number of sperms per ejaculate varied between 25 million and 600 million (average 257 million). The motility of the sperms was between 41 and 90% (average 73%). The vitality of the sperms, expressed by the number still alive 24 hours after the ejaculation, was between 6 and 30% (average 18.2%). The morphology of the sperms, considered one of the best criteria of fertility, was measured in terms of percentage of abnormal forms; 95% of the ejaculates showed abnormal forms in only 6 to 15% of the sperms. The author believes that the abnormal forms should not exceed 20%. Leukocytes were present in small number in 33% of the specimens, rare in 41%, and numerous in 26%. In four specimens the presence of mucus was observed, but no significance was attached to this finding. The presence of Bottcher's spermatic crystals, in examinations made 24 hours after the ejaculation, was noted in 15% of the specimens. Amylaceous corpuscles from the prostate were observed in only one specimen. These bodies are considered as an indication of exhaustion, although the patient claimed a complete abstinence of five days, as recommended by the laboratory.

COSTA RICA

Meeting of Central American Ministers of Health.—At the third meeting of Central American Ministers of Health held in San Jose, Costa Rica, in March, the four main points included in the agenda were as follows: 1. Coordination of the preventive medicine programs for all Central America. Isolated efforts to carry out good preventive programs, if properly coordinated, should give much more satisfactory results. 2. Creation of a Central American Institute of Intravenous Solutions and Vaccines. All Central American countries are spending vast sums for products that could be manufactured locally at a lower cost. 3. Facilities for personnel training. A reasonable number of institutions in this area have qualified technicians who could teach students from neighboring countries. This should relieve the shortage of qualified personnel and the difficulties (language and cost) of training all of them in the United States. 4. Creation of a Mental Health Institute. This would provide ample space for research as well as training in a field in which little advance has as yet been made in Central America.

FRANCE

Intramedullar Transfusions in Newborn.—Since 1945 Salvatore Folena (*Presse Méd.* **66**:641, 1958) has used a method of transfusion that is particularly useful in the newborn and the infant. The method consists in utilizing the transosseous and particularly the intrailiac route. The author concluded that the intrailiac could be substituted for the intravenous route when the approach to the veins appeared difficult, which was usual in the newborn. Furthermore the intrailiac route makes it possible to perform a direct transfusion (from the donor's vein to the bone marrow in the infant) and to avoid or reduce shock, as the injected fluid filters through the bone marrow before reaching the venous system. The ilium has a great absorptive capacity, behaving somewhat like a vast lacunar system communicating with the venous system.

Labyrinthine Vertigo.—J. Cellice and co-workers (*Presse Méd.* **66**:592, 1958) used ethanolamine acetyl leucinate (7452 RP) in the form of a 10% acid solution in the treatment of labyrinthine vertigo. This solution, which provokes neither local nor general secondary reactions, was injected intramuscularly or intravenously in doses of 0.5 to 1.0 Gm. of the active principle daily, for periods of from 10 to 15 days. In a series of 31 patients with vertigo due to various causes the authors obtained satisfactory results in 18. The best results were noted in patients with aural vertigo (success in 11 of 13 patients). The drug does not seem to lose its effectiveness and was efficacious against recurrences. On the other hand no improvement could be obtained with it in most patients with auditory hallucinations.

Cytochrome C as Metabolic Inhibitor.—H. Laborit and co-workers (*Presse. Med.* **66**:597, 1958) in a previous study demonstrated certain virtues of cytochrome C in animals. As a consequence of this study a solution containing a potassium salt of cytochrome C was prepared for use in man. This study led to the same conclusion: the solution of cytochrome C inhibited the velocity of cellular metabolism. It is, therefore, one of the rare agents capable of reducing metabolism without seriously disturbing respiration.

GERMANY

Genetic Aspects of the Neuroses.—P. E. Becker (*Dtsch. med. Wchnschr.* 83:612, 1958) stated that there has been a genuine increase in the incidence of neuroses in the last few decades; 40% of patients in a neurological practice had functional disorders, most of them neuroses. Factors predisposing to neurosis are acquired during early childhood; the mother plays the decisive role. An infantile emotional pattern and immaturity of the mother may initiate neurotic development. Abnormal irritability, emotional lability, and overprotectiveness may work in the same direction. Because such maternal emotional patterns are often in part genetically determined, the child's emotional structure may be similar. Such qualities as basic mood, sensitiveness, and initiative are largely genetically determined. It has also been shown that the actual neurosis is not inherited. Apart from the more general inherited neurotic disposition, genetic factors apparently play a decisive role in certain forms of neurosis. Thus studies of twins indicated a genetic factor in some cases of homosexuality. In addition, there is an acquired form of homosexuality. Parallel results were obtained in a study of enuresis (by Hallgren). In some cases there was a definite hereditary component. In some forms of addiction and organ neuroses a similar situation may exist.

Postnephritic Hypertension.—O. H. Arnold and K. D. Bock (*Dtsch. med. Wchnschr.* 83:711, 1958) reported a series of 14 patients, many of whom were followed for several years, after the acute phase of glomerulonephritis. In these patients the urinary signs of nephritis regressed completely, while arterial hypertension, indistinguishable from essential hypertension, became progressively more prominent. There was no evidence of abnormal renal function, as measured by the ability to concentrate and the absence of retention, of urea, for example, but para-aminohippuric acid and inulin clearances were normal in seven patients and abnormal in the remaining seven. Although there was in these patients no histological evidence that the renal disease had been cured, the clinical findings, characterized by the absence of all abnormalities in half of them, suggested that the persistent arterial hypertension should be considered a postnephritic hypertension. It is possible that in those patients in whom there was an abnormality in the clearance tests healing had occurred with residual defects. On the basis of results reported in the experimental reproduction of hypertension, a hypothesis is suggested for the pathogenesis of hypertension in the course of chronic glomerulonephritis.

Renal Involvement in Macroglobulinemia.—W. Schrade and co-workers (*Dtsch. med. Wchnschr.* 83:718, 1958) demonstrated small amounts of protein in three patients with macroglobulinemia, using the method of Bohler and Fischer, although sulfosalicylic acid had given negative results. Paper electrophoresis of the urine showed in addition to the albumin and ordinary globulin a prominent fraction which had the same migration velocity as the serum macroglobulin. Ultracentrifuge examinations in two cases showed that the various urinary protein fractions did not have a sedimentation constant greater than that of albumin. In a fourth case of macroglobulinemia, which clinically showed severe nephrotic syndrome and histologically gave evidence of advanced renal amyloidosis, abnormal proteins in addition to large amounts of normal proteins were probably present. The results indicated that as in multiple myeloma so also in macroglobulinemia there is a paraproteinuria; but in macroglobulinemia it is not marked enough to cause nephrosis. This is the reason why renal involvement is usually not a feature of macroglobulinemia, but in this condition, too, renal abnormalities may occur if there is deposition of amyloid in the kidneys.

JAPAN

Diphtheria.—The incidence of diphtheria has been increasing steadily. In 1953 there were 8,381 cases and 639 deaths. In 1956 there were 18,294 cases and 853 deaths. Heretofore it has been the practice to give diphtheria toxoid to the infants between 6 and 12 months old, but it has become apparent that the first immunizing dose should be given at about 3 months, when the immunity transferred from the mother is known to have disappeared. A booster injection is given at the age of about 1 year. A combined diphtheria toxoid and pertussis vaccine is used.

Infant Mortality.—In an effort to reduce the heavy death rate in infants better provisions are being made for the care of those born prematurely. Each year about 110,000, or 6.6%, of live births were premature. Of this number 22,000 babies died in their first year. To combat this situation (1) premature births must now be reported, (2) if the home conditions warrant it, the mother may keep the baby at home, being assisted by the visiting nurse and the midwife (incubators are supplied if needed), and (3) if the home conditions are inadequate the baby is removed to a hospital, at government expense if necessary.

Penicillin Shock.—A 45-year-old man was admitted with old extensive burn scars on the flexor surface of his left knee, with keloid changes in spots. He

had no subjective symptoms. A biopsy specimen of the scar was taken and the incision treated with penicillin solution. Shortly thereafter the patient showed signs of shock. He was given repeated blood and plasma transfusions and showed a temporary response, with momentary return of consciousness, only to sink into coma and die on the following day. It was later learned that the patient had had a similar but less severe reaction after taking penicillin several years ago.

Contraception.—Because of severe overcrowding the government about seven years ago sanctioned contraception and even the termination of pregnancy, in certain cases. The case fatality rate following interruption of pregnancy has been less than one per thousand, but morbidity rates are high, the commonest complications being hemorrhage, fever, and headaches. The number of patients so treated, according to the government records, are about a million annually, but half as many more are probably accounted for by private surgery. There is now a definite trend to discourage the interruption of pregnancy and to urge contraceptive measures. This requires educating the mothers by home instructions and group teachings. In this program midwives assist the social workers. In urban areas there has already been a 35% reduction in the birth rate. A similar change is expected in rural districts.

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PERU

New Medical Schools.—Exactly 102 years after the creation of the Faculty of Medicine of San Fernando of Lima, attached to the National University of San Marcos, two new medical schools were opened in Peru, one in Arequipa and the other in Trujillo. The Faculty of Medicine of the National University of San Agustin of Arequipa will admit not over 50 new students each year, all of them from southern Peru. This year only 42 applicants were found eligible. One of the best features of this new school is the loan of money to students who would otherwise be unable to attend.

Cancer of Uterine Cervix.—Dr. Mariano Bedoya Hevia, (*Ginecologia y Obstetricia*, vol. 3, Dec., 1957) reported a series of 52 patients with in situ or invasive cancer of the uterine cervix. He stated that total hysterectomy plus resection of one-third of both the vagina and parametrium, with or without bilateral oophorectomy, is the treatment of choice for stage 0 of epidermoid carcinoma or carcinoma in situ. The procedure selected in each case, however, must take into account the patient's age, parity, wish to have children, and presence or absence of associated genital lesions. In stage 1 of the invasive type of cancer, the therapeutic approach depends basically on the signs of sensitization response. Whether surgery or radiation is to be used rests on the results of this test. If operation is indicated, radical total hysterectomy plus lymph node resection should be performed. Irradiation is the method of choice for stage 2, except in patients showing a definitely poor radiation response. When the number of cells in vaginal smears displaying cytoplasmic vacuolization, nuclear changes, enlargement of both cell and nucleus, and multiple nuclei exceeds 60%, the response to radiation is regarded as poor. Radical hysterectomy with lymph node dissection is indicated for this type of patient. In stages 3 and 4 radiation continues to be the most effective treatment for most patients. Recurrences following this treatment call for pelvic exenteration. In carcinoma of the cervical stump operation is the best treatment unless definite contraindications exist. In pregnancy the management of cervical cancer depends on the viability of the fetus and the stage of development of the tumor.

Dehydration in Infants.—Dr. G. Morey and coworkers (*Revista del Hospital del Nino*, vol. 18, Dec. 1957) studied acute dehydration in 375 hospitalized children whose ages ranged from 0 to 3 months in 41 (10.94%), 3 to 6 months in 86 (22.94%), 6 to 9 months in 72 (19.21%), 9 to 12 months in 87 (23.20%), and 1 to 3 years in the remaining 89 patients (23.71%). All had a history of vomiting and diarrhea; 250 (66.67%) showed on admission severe involvement of the nervous system manifested by notable impairment of the sensorium; 42 (11.72%), abdominal distension; 35 (9.33%), muscular hypotonia; 32 (8.52%), generalized edema; and 17 (4.52%), marked restlessness. Only 107 children (28.53%) were found to be lucid on admission. Most patients (82.1%) were febrile, and 216 children (62.56%) were in shock. On admission, the body weight, as compared to the ideal, showed a deficit of 0% in 19 (5.1%), of from 1 to 25% in 100 (26.6%), of from 25.1 to 50% in 212 (56.6%), and of more than 50% in the remaining 44 (11.7%). Secondary infections, chiefly of the respiratory tract, occurred in near 33% of the patients.

Hypertonic saline solution, given intravenously in concentrations based on pretreatment serum electrolyte determinations was the principal treatment. The amount of fluids given per day per kilogram of body weight varied between 100 and 250 cc. Fluid retention 24 hours after the onset of rehydration therapy ranged from 1 to 10% of the total amount of fluids given to 206 patients, from 11 to 20% of that given to 91, and exceeded 20% of that given to 12. These figures do not include two patients who died within the first 24 hours and 64 who showed negative fluid balances in this period. Supportive antibiotic therapy, usually chloramphenicol, was given to all patients.

In this series 101 of the patients died, a case fatality rate of 26.93% as compared with 57.5% in 1956. This improvement is the result of earlier recognition and treatment and more accurate use of replacement solutions. In 65 of the fatal cases, death was caused by complicating infections. Thus the primary condition accounted directly for the death of only 9.6% of the entire group. No statistically significant relationships were found between the case fatality rates and the severity or duration of the disease prior to hospitalization, but the authors got the impression that the deaths were more closely related to severity than to duration. No significant relationship was observed between the case fatality rates and the volumes of fluid given per day per kilogram provided this was at least 100 cc. The case fatality rates in the few children given 301 to 380 cc. per day per kilogram did not differ significantly from those of the groups receiving the smaller, conventional quantities of fluids. No signs of overhydration were noted in such patients. No significant relationship was observed between the case fatality rates and the percentage of fluid retention following therapy, but none of the patients with over 20% fluid retention died. A notably higher case fatality rate was, however, noted in those patients coming to the hospital with clouded sensorium or in severe shock.

UNITED KINGDOM

Incidence of Sonne Dysentery.—Sonne dysentery is now a major public health problem in the United Kingdom, and in 1956 the number of reported cases reached its highest level, 49,009. W. H. Bradley and co-workers (*M. Officer* **99**:175, 1958) noted that this increase in incidence was accompanied by a fall in the case fatality rate. In 1925, this rate was 39.1%, compared with 0.1% in 1956. In recent years, practically all the dysentery in England and Wales has been due to Shigella sonnei. The number of reported cases per 100,000 are much higher in the age group 0 to 4 (458.8 in 1956) than in the age group 5 to 14 years (288.5), and the incidence in the latter period was much higher than that observed in those 15 years of age or more (37.5). It is definitely a disease of the colder rather than the warmer months. Before 1947 it was relatively more prevalent in rural and similar areas, but lately it has been more prevalent in urban areas. As, unlike Shigella flexneri, the strains of Sh. sonnei are antigenically homogenous, no useful epidemiological information was obtained through serotyping of strains. Recently attention has been paid to the occurrence of sulfonamide-sensitive and sulfonamide-resistant strains. In many epidemics the strains of Sh. sonnei have the same sensitivities, but outbreaks in neighboring areas may have the same or different sensitivities. There is little support for the idea that a progressive replacement of sensitive by resistant strains is taking place. As in cases in which the strain is sensitive bacteriological cure is more easily and rapidly ensured if the patient is vigorously treated in the acute stage of the illness, it is recommended that, at intervals in an outbreak, organisms isolated from a small number of patients be tested for sensitivity to make sure that there has been no change and that they are sensitive to the preparations being used in treatment. Strains resistant to streptomycin and oxytetracycline have also been observed, but so far only infrequently.

A feature of Sonne dysentery is its clinical mildness, particularly in adults in whom the only evidence of infection may be one or two loose stools, with no other signs or symptoms. The frequency and extent of the spread suggests that the infecting dose of organisms is very small. Until recently attention has been focused mainly on day nurseries as places where the disease is spread. It has become increasingly apparent, however, that kindergartens are of great importance in the dissemination of the infection. The infected children pass the infection on to siblings and parents at home, although at times families may be the prime cause of spread of the infection. Except in special circumstances, there is little evidence to support the thesis that anything is to be gained from the addition of sulfonamide prophylaxis to the preventive measures normally used.

Coronary Thrombosis.—One of the few towns in which coronary thrombosis is reportable is Kilmarnock, a burgh of 44,000 inhabitants in Scotland. In his annual report, the local health officer stated that there were 110 coronary attacks in 1956. There were 74 first attacks, of which 50 were fatal, and 36 subsequent attacks, of which 15 were fatal. The available evidence did not suggest any connection between the excessive consumption of alcohol and coronary thrombosis. Most of the men were smokers, many of them heavy smokers, but in the case of women it was the exception to find any who smoked at all. Most of those affected were excitable rather than placid. Of the deaths among men 67% occurred within 24 hours of the onset, and the proportion in the women was even higher. While the number of men having a frank thrombosis as the first manifestation, as compared with anginal pains, was about equal, among the women nearly four times as many had thrombosis as a first manifestation as had anginal attacks. This was correlated with the fact that the mortality in women (33 of 40) was higher than that among the men (32 of 70).

Home Contacts of Poliomyelitis.—The Public Health Laboratory Service (*Month. Bull. Min. Health* **17**:58, 1958) examined the stools of 96 pa-

tients with poliomyelitis and 290 household contacts in the summer and autumn of 1956. The finding of virus in the contacts was associated (1) not with the occurrence of paralysis in the patient but with the excretion of virus in the patient's feces and (2) with the age of the contact; the younger the contact, the more likely was virus to be found in the feces. Thus, under 5 years of age the proportion of excretors among the contact was 63%, between 5 and 15 years 36%, and over 15 years 9%. The proportion was higher in contacts of patients who were shown to be excreting virus than in those who were not (30%, compared with 18%). The elapsed time between the onset of illness in the primary case and the examination of feces from the contacts made little difference to the chances of finding the virus; the proportion was just as high in specimens examined three or four weeks after the onset as during the first week. Irrespective of which is the commoner method of infection, it seems clear that in any household in which one member develops poliomyelitis a large proportion of the other members are infected too. In children under 5 years of age this proportion probably approaches 100%. Whatever therefore may be said for segregating these children, there is practically nothing to be said for protecting them with gamma globulin.

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Tuberculin Tests.—The tuberculin subcommittee of the research committee of the British Tuberculosis Association (*Tubercle* **39:**76, 1958) compared the Mantoux, Heaf, von Pirquet, and jelly tuberculin tests. The comparisons were based on the effectiveness of the tests in detecting positive reactions, their reproducibility, their ease of performance, the consistency of the results recorded independently by two observers, and the confidence of the observer in the result recorded. On all of these points, the Mantoux and Heaf tests were found to be superior to the other two. On the other hand, blistering was more often recorded with the Mantoux and Heaf tests than with the other two. The jelly test was unreliable, difficult to perform, and hard to read. The sole recommendation of this test is that it requires no needle or skin puncture, but in the light of the accumulated evidence against it it should be abandoned. The von Pirquet test showed surprisingly poor results in this trial. The Mantoux test, using 5 units, yielded a slightly higher percentage of positives than the Heaf test. On the other hand, the Heaf test was preferred by 80% of the clinicians using both tests. Both tests gave highly reproducible results and showed little variation between the readings of the two observers. On the whole, the observers were more confident in their readings of the results of the Heaf test than in their readings of the Mantoux test, but this may be related to the fact that the Mantoux test result had to be recorded in millimeters and the Heaf test simply in one of four grades. Both tests with 5 units of tuberculin may therefore be regarded as being suitable as single tests for large-scale epidemiological work.

Psychosis due to Antituberculous Drugs.—E. H. Hare (*Tubercle* **39:**90, 1958) reports a series of four patients admitted to a mental hospital on account of psychotic reactions attributable to the use of antituberculosis drugs. In one, confusion and choreiform movements arose after four weeks' treatment with streptomycin and persisted for four weeks after the drug was withdrawn. The second developed a toxic-confusional state after three weeks' treatment with streptomycin. This persisted for four weeks after withdrawal of the drug. In the third patient, auditory hallucinations and depression developed after four months of therapy with isoniazid and were still present two years after the drug had been withheld. The fourth patient developed auditory hallucinations after nine months' treatment with isoniazid. They persisted for six months after the drug was withdrawn. None of these patients had a previous history of psychotic or neurotic behavior, and only the fourth had a positive family history. It was concluded that if mental disturbance develops during antituberculosis treatment with streptomycin or isoniazid, it is reasonable to assume that the drugs may be responsible, and that, of the two drugs, isoniazid is more likely to be the cause and in general, therefore, should be the first to be withheld. Because psychosis associated with isoniazid may be prolonged, manifest mental changes in patients on isoniazid therapy should, in general, be an indication for withdrawing the drug.

Cycloserine in Pulmonary Tuberculosis.—On the basis of their experience with cycloserine in the treatment of 16 patients with advanced and drug-resistant cases of pulmonary tuberculosis, M. Weinberger and co-workers (*Tubercle* **39:**96, 1958) concluded that cycloserine might be useful in patients who failed to respond to other forms of chemotherapy or whose tubercle bacilli were drug-resistant, but that great care was necessary in the selection of patients, and the dosage should not exceed 750 mg. daily. Of 11 patients in their series who completed three months of treatment, 10 improved clinically, 3 showed radiological improvement, and sputum conversion occurred in 1. Six showed a reduction of tubercle bacilli in the sputum after three months, but two of these reverted to their previous status in spite of therapy with cycloserine being continued Serious convulsions occurred in three patients, with one death. One other patient died of myocardial failure, but it is doubtful that his death was attributable to cycloserine. This drug has the advantage that it

is effective by mouth without causing any untoward gastrointestinal symptoms, but the therapeutic dose is too close to the toxic dose for the drug to be used routinely, and it cannot be regarded as a substitute for standard antituberculous drugs.

Hazards of Mass Roentgenography.—In *Tubercle* (**39**:116, 1958) much criticism was expressed concerning a memorandum on the development of mass miniature roentgenography, published by the Ministry of Health last year. The main criticism was of the absence of any reference to the hazards of this procedure. Although the hazards may be small, there is a danger that chest physicians and surgeons may become careless about it. The dose received by the female gonads has already been shown to be greater for small films than for large ones, and the measurements so far for the skin dosage, comparing large and small films, have been found to be in a ratio of 1:4 or more. This should be taken into account in discussions as to whether large or small films should be used.

Boxer's 321 Days in Coma.—At an inquest at Manchester a verdict of death by misadventure was recorded on a 23-year-old boxer who died after being in a coma for 321 days after a bout. He had collapsed in his dressing room shortly after being felled by two blows on the jaw. He had previously sustained a head injury in an Army boxing match and had been warned to give up boxing on account of this. Two operations had been attempted on the brain. At the autopsy no fracture of the skull was evident and there was no laceration of the surface of the brain. The meninges were thickened and stained, suggesting a previous hemorrhage, but there was no sign of a recent one. Death was due to bronchopneumonia following internal hydrocephalus caused by traumatic subdural and subarachnoid hemorrhages. According to the pathologist the condition, which was comparatively rare, could have been caused by blows on the jaw.

Industrial Health Service.—In Slough, an industrial area just outside London, many factories are concentrated in a small area, which is suited for the establishment of the cooperative type of industrial health service. The Slough Industrial Health Service, which is independent of any national scheme, was started in 1947. The current annual report surveys the first 10 years' working of the service. When it began the membership included 52 firms with 6,324 employees. Now there are 179 member firms with 17,748 employees. The service provides medical care for those factories that are too small to support a full-time medical officer and nursing service. The medical care of employees of member firms with no medical department of their own costs about $6 a head per year. Half of this pays for the casualty service, which treats about 500 cases a day, 98% of whom are able to resume work after treatment. About 0.8% of those attending are referred for hospital treatment. An orthopedic surgeon, a plastic surgeon in charge of the hand clinic, a cardiologist, a dermatologist, and an industrial medical officer hold regular clinics. There is also a mobile dressing station which visits out-of-the-way factories and thus saves the time of the worker. The clinics are provided with roentgenological, pathological, physiotherapeutic, and social services. There is a rehabilitation center at Farnham Park. The health service also provides an occupational hygiene service, which, in collaboration with the London School of Hygiene and Tropical Medicine, advises on and investigates environmental conditions in the factories. Initial and periodic medical examinations and annual examination of senior executives are also carried out as part of the service.

Fat Mobilizing Factor in Urine.—Chalmers and coworkers (*Lancet* **1**:866, 1958) showed that the urine of healthy fasting subjects contains a factor that mobilizes fat in experimental animals, increases the amount of fat in the liver, and increases the total metabolic turnover of body fat. It causes loss of weight without depressing appetite, the loss being in the form of body fat and water. Normal subjects fasted for 36 hours, and their urine was collected during the last 24 hours of this period. It was acidified to pH 5.3 and treated with 2 volumes of alcohol. The precipitate that formed in the next 24 hours was separated by filtration, washed, dried, and extracted with 0.5% sodium carbonate solution. The alkaline extract was reprecipitated at pH 5.3 with alcohol and the previous process repeated. The volume of extract was adjusted to 10 ml. for a 24-hour specimen. Mice, which were used as test animals, showed an increase of liver fat when given 0.5 ml. of the extract subcutaneously. With glyceryl tripalmitate, labelled with C^{14}, as a source of fat, it was shown that the extract did not merely transfer fat from the depots to the blood stream and liver but also increased the rate of fat metabolism in the body. After injecting the urine extract from normal subjects in the fasting state, not more than 25% of the administered activity of the glyceryl tripalmitate could be recovered as fat. As the total amount of fat in the animals was not less than in controls, it would appear that the total metabolic turnover of fat was increased in the animal as a whole. The injected mice also lost an average of 6 Gm. each over a 17-day period. Analysis of the carcasses and comparison with controls showed that this was due to loss of body fat and water. The active material was partially purified by paper chromatography. It was only present in the urine of fasting subjects or of subjects given a high fat or high protein diet. It was absent in those given a diet in which calories were supplied in the form of carbohydrate.

Allergic Reactions Abolished by Hypnosis.—The successful relief of the symptoms of allergic skin reactions by hypnosis was reported by Mason and Black (*Lancet* 1:877, 1958). A woman with a history of severe and intractable asthma and hay fever of 12 years' standing was found on skin testing to be sensitive to extracts of pollens of grasses, trees, and spring flowers. The attacks occurred only between May and July. As the patient refused desensitization an attempt was made to treat her by hypnosis. A week before the yearly attacks of asthma and hay fever were due she was put into a trance and told she would have neither asthma nor hay fever attacks in the coming season and that she would no longer be sensitive to skin tests for pollens and other substances in the atmosphere. Hypnotic treatment was given from April to July, and during the whole of this period the patient remained free for the first time in 12 years from attacks of asthma and hay fever. Weekly skin tests were made during this period with the allergens to which she was sensitive. The skin reactions slowly decreased each week until by the seventh week they could no longer be elicited in the arm, although they could in the thigh. Further suggestion was made that skin sensitivity would disappear over the whole body. This happened by the ninth week. An attempt was then made to elicit the Prausnitz-Küstner reaction in a nonallergic volunteer by intradermal injection of the patient's serum and subsequent skin testing with the allergens to which the patient was known to be formerly skin sensitive. After 30 minutes there was a skin response to extracts of pollen of grasses and trees. Thus with the patient now free from both allergic symptoms and skin reactions, it was still possible to produce the Prausnitz-Küstner reaction in the skin of a volunteer normally insensitive to the allergens. The symptoms of physical illness were removed by hypnosis, although the patient's blood still contained the serologic basis of her previous hypersensitivity in the form of passively transferable antibodies or atopic reagins.

Subsidized Medical Students.—Mr. Harold Edwards, representing the Royal College of Surgeons said that a different type of person is studying medicine today. Whereas 20 years ago only 27% of medical students received scholarships today 74% receive financial aid from government or university grants. The proportion is even higher among dental students. This results in selection of those who are apt scholars, but these students do not necessarily make the best physicians. The practitioner of today is not a mere machine. The art of medicine and surgery looks more and more to the basic medical sciences, and if the practitioner is to keep abreast of advancing knowledge he needs leisure to read, write, and travel. These are traditional obligations to his art, and they are expensive. He must therefore be able to look forward to a standard of professional earnings which allows him to incur such expenditure. If he is so "squeezed" that these essential activities are no longer possible, the quality and prestige of British medical and surgical practice will decline.

WORLD HEALTH ORGANIZATION

Poliomyelitis.—Virus diseases affecting the nervous system are a growing problem in Europe. Particularly regarding poliomyelitis, more information on the occurrence of the disease is needed. In many countries reliable data are not available and underreporting is general. To obtain a true picture of the importance of poliomyelitis it is necessary also to consider the accumulation of paralytic cases. Each year a new group of cases of permanent paralysis is added to the large numbers remaining from earlier years. The Study Group on the Control of Neurotropic Virus Diseases, which met in Copenhagen in April, recommended that the true medical, social, and economic consequences of poliomyelitis be determined.

Epidemic waves of poliomyelitis occur every few years and, because of this periodicity, it is too early to be quite certain about the value of mass vaccination campaigns against poliomyelitis, but the incidence of paralysis has declined after such campaigns, and this fact justifies the continuation of campaigns or the starting of new campaigns in countries where poliomyelitis is important. In countries where insufficient information is available more precise data should be obtained before an expensive vaccination program is undertaken. It will also be necessary to consider the results likely to be obtained in relation to the other demands on the limited resources available for health programs in some countries. Accidents after the use of poliomyelitis vaccine have been few because of the great care taken during vaccine production and testing. Although results with live poliovirus vaccines have been promising, these vaccines are still experimental and the group recommends caution in their experimental use.

Virus diagnostic laboratory services should be made available in all countries (1) to inform the public health authorities of disease-causing viruses existing in the country, which will enable them to take appropriate preventive action, (2) to assist in making epidemiological investigations and to improve the reporting of communicable diseases, (3) to evaluate control measures, and (4) to ensure the proper approach to prevention and the early treatment of disease. Though specific laboratory diagnosis of most virus diseases may be of little value for individual cases, an efficient laboratory service may be able to provide useful pointers to the physician in charge of the patient.

CORRESPONDENCE

ACCIDENTAL DROWNING

To the Editor:—It may be timely, with the swimming season about to start, to scrutinize the possible causes of accidental drowning. Being interested in recreational therapy for cardiacs, we at the Valley Forge Heart Hospital & Medical Center encourage water sports, among various activities, for patients with arrested rheumatic heart disease, hypertension, atherosclerosis obliterans, and congenital heart disease (classes I, II, A, and B, according to the classification of the American Heart Association). These activities are engaged in only under the careful supervision of the physician.

In reviewing records covering a period of 25 years at the Wolffe Clinic, Philadelphia, and the Valley Forge Heart Hospital, Fairview Village, Pa., with an average case load of 1,400 new cases per year, we found six instances of accidental drownings or near-drownings. On the basis of mere impressions, these accidents could have been attributed to heart disease. In all of these instances searching histories following the accident revealed preexisting grand mal and petit mal in cardiac and noncardiac patients.

In one patient, ventricular fibrillation was considered as a cause rather than an effect. No cardiac pathology was found at autopsy. The case of one boy may well illustrate the point. He drowned while practicing in a university pool in June, 1956. In 1955, while attending another college, he had been considered one of the top free stylers in swimming history. In August, 1955, he had been in training for the Olympic tryouts and was one of the nation's brightest prospects.

In June of 1956, while training for the Olympics, he splashed to a stop in midstroke at the shallow end of the pool and grasped the gutter with both hands. He slumped back into the water with his eyes closed. Swimmers lifted him to the deck face down. He groaned a few times but did not respond to artificial respiration and the use of a Pulmotor. It was certified that the cause of death was "acute cardiac arrest while swimming." A physician from this school's department of health stated in a personal communication: "I am sorry to say that a careful scrutiny of the tissue at postmortem failed to uncover any suggestion of antemortem breakdown. It is assumed that ventricular fibrillation supervened, but the cause remains Deus Ex Machina."

The electrocardiogram of another patient after near drowning showed numerous ventricular ectopic beats occurring in rapid succession. This may be the mechanism which ushers in ventricular fibrillation when one or more ectopic foci assume control and become the cardiac pacemakers. Defibrillators may be lifesaving when available.

A young mother drowned in a bathtub while bathing her child. She had a slight mitral insufficiency but also suffered from grand mal. Yet, the death certificate read, "drowned during heart attack." Since there are more than half a million epileptics in the United States, it is unknown how many accidental drownings attributed to heart failure were due to grand mal and petit mal seizures while swimming or being near water.

Since an accidental drowning, apparently due to an epileptic seizure, in a Y.M.C.A. pool, the director of physical education does not permit epileptics the use of the pool, regardless of individual or parental pressure. Students in the field of epilepsy feel that this is not warranted, particularly when the physician has the patient under good medical control. According to some authorities, epileptics under supervision are safe where normal persons are completely safe. However, a very careful history, particularly in reference to recurring convulsive seizures, might be one way of reducing the number of accidental drownings.

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STAPHYLOCOCCIC INFECTIONS

To the Editor:—Recent articles in The Journal on staphylococcic infections in hospitals have been widely discussed. This situation should give an important warning to physicians regarding hospitalization of patients for diagnostic studies. There probably is some risk to such patients. Therefore physicians should think twice before hospitalizing patients on some nebulous diagnosis in order to get an insurance company to pay for a diagnostic examination that could well have been done on the outside. We physicians, without being alarmists, can gently wean patients away from such unnecessary hospitalization.

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MISCELLANY

AMERICAN COLLEGE OF PHYSICIANS MEETING

Once again the chemotherapeutic revolution of the last 15 or 20 years came under the close scrutiny of the American College of Physicians. Dr. Howard Wakefield, of Chicago, was emphatic in condemning routine use of any drugs. When medicine can be practiced by formula it ceases to be an art or a science and becomes merely skilled labor. Individualization is essential in treating any condition, because no drug has the same effect on all persons and may even have different effects on the same person at different times. He particularly condemned the routine use of anticoagulants and emphasized the need for careful differentiation between the pain of a coronary occlusion and that of a perforated peptic ulcer, since more than one patient with the latter condition has suffered a fatal hemorrhage as a result of taking anticoagulants. In a panel on the tranquilizers, it was noted that, although these drugs are indicated chiefly in the treatment of psychoses, they have come to be used on millions of nonpsychotic patients. Dr. Edward Weiss, of Philadelphia, said that often a physician develops a feeling of hostility toward a patient who has a functional illness or an illness that does not respond promptly to treatment. In such a situation there is a great temptation to give the patient a tranquilizer. This amounts to putting the patient in a chemical strait jacket and is a highly questionable procedure. Dr. Weiss concluded that the more a physician gives of himself the less need he will have to prescribe tranquilizers.

A similar note was struck by the panel on life situations, emotions, and the gastrointestinal tract; it was concluded that, when a patient shows antagonism to a physician by such complaints as "I've been coming to you for a long time and I'm not a bit better," the physician must not react in kind by rejecting the patient. He must not, for example, say, "Well, then, why don't you go to someone else?" or "I have done all that I can for you." Surely, no physician is likely to react in this way toward a patient he knows is dying of cancer. Refusal to reject the patient is in itself a powerful therapeutic tool. When there is a genuine feeling for the patient's welfare, the patient senses this and is thereby given a support he greatly needs. Another potent therapeutic measure that should never be omitted is to give the patient a simple physiological explanation of the cause of his symptoms couched in language he can understand.

In delivering the John Phillips Memorial Lecture, Dr. Amos Christie, of Nashville, Tenn., said that since the introduction in 1945 of the histoplasmin skin test as a case-finding tool and as a means of establishing an epidemiological index human histoplasmosis has emerged from a category of rare disease to one which must be considered in any case where hepatosplenomegaly, fever, ulceration of the skin and mucosa, and pulmonary lesions are otherwise unexplained. Prior to 1945, histoplasmosis was considered to be a uniformly fatal disease. It has now been established that there are many benign but symptomatic cases, and these are frequently recognized when one's index of suspicion is high and when currently available laboratory aids are used. The geographic distribution is also much wider than previously recognized. Histoplasmotic meningitis simulates the meningitis of tuberculosis. Histoplasmotic involvement of the adrenals has also been observed. The only chemotherapeutic agents of any value are some of the sulfonamides.

Influenza.—Dr. Gordon Meiklejohn, of Denver, stated that the chief problem remaining to be solved in influenza appears to be that of preparing a vaccine that would protect not only against influenza virus strains current in the past but also against new variants. The situation which existed when Asian strains of influenza A were first isolated appeared particularly promising because there was time to prepare in advance a strictly homologous vaccine for the epidemic that was expected. It soon became clear, however, that with vaccines for Asian strains of potency comparable to those used in earlier studies in single injections the antibody response was far less satisfactory than had been anticipated. In retrospect, it is clear that the schedule of single-injection immunization which has been followed in the past was unsatisfactory and that a double or booster type of immunization schedule produced a far better antibody response. Time did not permit the use of this type of program. It was concluded that the most promising approach to protection against any type of influenza A or B would be to prepare a vaccine containing all the major families of each virus. If there are only four or five main families within the influenza A group this would not be too formidable a task, as polyvalent adjuvant vaccines could be used to provide immunization against these major families. Appropriate booster injections could then be given at suitable intervals and a much higher degree of protection obtained in the future than has been observed in the past.

Apoplexy.—Harold Stevens, of Washington, D. C., reported that the spontaneous occurrence of cerebrovascular accidents in normotensive, apparently healthy persons is not as rare as was once believed. He encountered 32 such cases in young adults and 2 in children. Acute hemiplegia and other focal neurological manifestations characterized this group. All subjects were ambulatory and active. Most were white-collar workers. Although

the precise mechanism was not always established, two large categories of strokes in young persons were recognized: those due to venous thrombosis, including infantile hemiplegia, puerperal hemiplegia, and the venous thrombosis of pregnancy, and those due to arterial thrombosis, including thrombosis of the carotid, middle cerebral, and circle of Willis arteries, singly or in combination. Infantile hemiplegia may occur spontaneously but almost always is associated with fever or dehydration. Puerperal hemiplegia is probably the commonest form of spontaneous stroke in healthy women. The precise mechanism is unknown, and it is only in recent years that this condition has been recognized during life. A similar but less common affliction may occur in early pregnancy.

In patients with thrombosis of the carotid artery the indiscriminate use of arteriography is not justified, since the diagnosis can often be made on clinical grounds and the arteriogram does not always reveal the occlusion. Thus, responsibility for refining the diagnosis of strokes in the young reverts to the clinician, on whom it rested before Moniz introduced arteriography in 1927. It is often impossible on clinical evidence alone to distinguish between middle cerebral and carotid artery thrombosis. The presence of a Horner's sign (Spaulding's sign), with contralateral hemiplegia and decreased pulsation of the carotid artery, establishes the latter on clinical grounds. Surgical measures for thrombosis of the middle cerebral artery are rarely necessary, in view of the favorable outcome observed with conservative treatment in nearly all cases of cerebral thrombosis. Surgery on the carotid artery is still in the investigative stage but may evolve into a safer and more satisfactory procedure in the future. The cause of cerebral arterial thrombosis is atheromata, analogous to, if not identical with, the atheromatous process that occurs in coronary vessels and elsewhere.

Plaques that cause strokes in the young, apparently healthy, normotensive person are probably solitary. This assumption seems plausible since none of these patients died, residuals were uncommon, and practically all returned to productive work. As in coronary artery occlusion in persons in a comparable age group, the patients were predominantly male. It seems reasonable to give these patients anticoagulants if cerebral arterial thrombosis has occurred or is threatening. Millikan and co-workers have documented their arguments for this measure but insist on restricting anticoagulant therapy to those with (1) intermittent insufficiency in the vertebral-basilar system, (2) intermittent insufficiency in the carotid system, (3) thrombosis in the vertebral-basilar system with infarction, and (4) actively advancing thromboses in the carotid system. Effective treatment of strokes requires exacting refinement of diagnosis and detailed attention to the patient's age, presence of underlying cardiovascular or thromboembolic disease, metabolic disorders, malignancy, subarachnoid bleeding, site of the lesion, and other variables. A stereotyped therapeutic approach is hazardous to the patient.

Aviation Safety.—Dr. Howard T. Karsner, of Washington, D. C., said that improvements in the safe operation of aircraft in recent years have been great. It is well known that many accidents are not due to faults in the engines or airframe. When this is true, the medical aspects of the accident must be considered. Pilot error and accidents may, in general, result from the pilot's physiological tolerances, his behavioral variances, and his physical condition. The pathologist may play a part in all of these areas, but he attacks the problems under different headings, namely (1) preexisting disease, (2) traumatic factors, and (3) environmental factors. The performance of an autopsy when an aircrew fatality occurs usually determines whether there was a preexisting disease, even when the history is not contributory, but the pathologist must know all the circumstances of the crash in order to justify a belief or a conviction that the disorder was a cause of pilot error or failure. The mere fact that a crew member has profound coronary atherosclerosis does not necessarily mean that this caused pilot failure, because young men may have this disease without notable disability. The pathologist should add his evidence to that of the sequence of events in a reconstruction of the accident. The autopsy is not complete without a thorough study of the traumatic forces. There should be a correlation of the observations of the pathologist with the adequacy of protective equipment, such as helmets, restraint devices, and design of the aircraft for crash-worthiness.

The introduction of high-performance jet aircraft into the services has had a definite impact on the accident rate, and it is possible that something of the same sort may eventuate when jet planes are used in large numbers in civil aviation. Even in the services jet planes are in the minority, but they account for 62% of pilot fatalities in the Air Force and 53% in the Navy. This refers to fatalities rather than to accidents. The training of a pilot costs at least $100,000. When he has a fatal or disabling accident, that money is sacrificed—as is also the large cost of the airplane.

Environmental Forces.—Drs. Lawrence E. Hinkle Jr. and Harold G. Wolff, of New York, stated that by the beginning of the present decade there was ample proof that a man's reactions to the situations that he encounters in his daily life may affect a great number of his internal processes, a fact that had long been recognized clinically. On the other hand, the extent to which such adaptive reactions are involved in disease in general and the degree to which they determine the health of the individual remained to be established. For this reason, a series of more than 3,000 persons, drawn from the ambulatory population, has been studied. This

sample included two American working groups that had long-term, unbroken, comprehensive records of health, attendance, and performance at work. The groups were also remarkably homogeneous with respect to many characteristics of their members and the environment in which they had lived. Most of them had spent their young adult lives in a social milieu that did not undergo dramatic change. Among these persons, therefore, the individual life experience was a prominent variable. The Chinese, by contrast, had spent their lives in an environment that was undergoing dramatic social and cultural change, and their individual experiences included a variety of geographic, political, and economic dislocations, as well as difficulties arising from interpersonal relations. The American college graduates and the Hungarian refugees had still different sets of characteristics and experiences.

The information derived from this study indicated that, whoever a man might be and whatever might happen to him, the way that he perceived his life situation and reacted to it was an important determinant of his health. At least 33% of all the illness episodes that occurred among these persons were influenced in their time of occurrence, or in their course, by the attempts of the individual to adapt to the events and situations that he encountered. This estimate was based on the occurrence of clusters of episodes and their demonstrated relationship to life experiences. Persons with a consistently high illness rate showed a continuing inability to make an adequate adaptation to their environment. When this additional point is considered, it seems likely that efforts to adapt to the social environment are to some degree involved in most of the illness episodes that occur among adults. Some illnesses are undoubtedly influenced in this manner much more readily and to a much greater degree than others. Illnesses so easily influenced have been called "psychosomatic," but these studies yielded no evidence to support the idea that there is any special category of diseases which should be designated by this unfortunate term.

In his presidential address, Dr. Richard A. Kern, of Philadelphia, stressed the role of the physician as a citizen and the need of the community for his active participation in civic affairs. Special honors were conferred on Chester M. Jones of Boston; Walter B. Martin of Norfolk, Va., who is an ex-president of the American Medical Association; T. Grier Miller of Philadelphia; Jonas E. Salk of Pittsburg; Maurice C. Pincoffs of Baltimore, who has completed 25 years as editor of the *Annals of Internal Medicine;* Amos Christie of Nashville; Alexander M. Burgess of Providence; and Eduardo Braun-Menendez of Buenos Aires. Dr. Braun-Menendez has succeeded Dr. Bernardo A. Houssay as head of the Instituto de Biologia y Medicina Experimental.

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MEDICAL FILM REVIEWS

Surgical Correction of Vaginal Agenesis Utilizing Skin Graft: 16 mm., color, sound, showing time 10 minutes. Prepared by Albert Altchek, M.D., and Jacob Shragowitz, M.D., New York. Produced in 1957 by Sturgis Grant Productions, New York, with a grant from Parke Davis and Co. Procurable on rental or purchase from Mr. Robert Duckworth, Grasslands Hospital, Valhalla, N. Y.

The purpose of this film is to demonstrate the authors' technique of constructing an artificial vagina in a one-stage procedure by utilizing a split-thickness skin graft. An intravenous pyelogram reveals an anomalous double left kidney and double ureter, and a skin biopsy shows genetic female sex chromatin. Various molds and measurements are demonstrated, and a split-thickness graft is taken from the inner aspect of the left thigh with an electrodermatome. This is sewn over the mold and packed into newly created space. The mold is removed 11 days postoperatively, and a follow-up examination at 15 weeks is demonstrated. The surgical principles are excellent. The technique is good, and the only possible adverse criticism is that in the dissection of the space between the rectum and the vagina not enough detail is shown. The photography and sound are excellent. This film may unhesitatingly be recommended to any surgeon with the skill requisite to manufacture an artificial vagina.

Reach into Silence: 16 mm., color, sound, showing time 13 minutes. Produced in 1957 by Department of Cinema, University of Southern California, under a grant from the Beltone Hearing Aid Company. Presented by the John Tracy Clinic, Los Angeles. Procurable on loan from Harshe Rotman, Inc., 8 S. Dearborn St., Chicago 3.

The methods used at the John Tracy Clinic to train teachers for the difficult job of helping deaf children to speak are shown in this film. It follows a typical college student named Betty from the time she decides to be a teacher of the deaf to the day she completes her training. It shows much of her actual schooling at the clinic, the equipment she learns to use, and her observations of graduates working with the children on lip movements, sounds, and vibrations. It also shows her frustrations and disappointments when the child fails to respond but points out her feeling of satisfaction and excitement when communication with the child is finally accomplished. This is an outstanding film for use in recruitment of teachers of the deaf. It would give prospective teachers a good picture of some of the things they would be doing, particularly in regard to auditory training and audiometric testing. The presentation is appealing, and the techniques of teaching young deaf children are well demonstrated. It would be especially helpful in recruitment of teachers from high school seniors and college freshmen and sophomores.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Acute Thrombosis of the Renal Vein in an Adult. N. Naeraas. Ugesk. læger **120**:186-189 (Feb. 6) 1958 (In Danish) [Copenhagen].

A case of acute thrombosis of the renal vein in a man, aged 50 years, with previously healthy kidneys is reported. During the course of a pneumonia severe symptoms from the urinary tract set in: macroscopic hematuria, albuminuria, cylindruria, and colic-like pain in the left side of the abdomen. Death occurred 23 days after the development of the renal symptoms, from massive embolism in the pulmonary artery. Autopsy showed, in addition to the pneumonia in the lower lobe of the left lung, massive hemorrhagic infarction of the left kidney with extensive thrombus formation in the entire renal vein. In the right kidney there were some capillary thrombi, no infarction. Diagnosis was not made till autopsy. The clinical diagnosis was hypernephroma with pulmonary metastases. In the literature 291 cases of thrombosis of the renal vein have been published. Treatment consists in combating the condition of shock and nephrectomy as soon as possible. Nephrectomy was done in 37 cases, with recovery in 29. In the last 10 years 12 cases of unilateral thrombosis of the renal vein in infants have been reported, all diagnosed and treated operatively with success.

A Study of Cardiopulmonary Alterations in Patients with Sickle Cell Disease and Its Variants. B. J. Sproule, E. R. Halden and W. F. Miller. J. Clin. Invest. **37**:486-495 (March) 1958 [New York].

A high proportion of individuals who possess S-type hemoglobin exhibit significant desaturation of the arterial blood. The exact mechanism responsible for this phenomenon has not been elucidated. The authors describe studies carried out in an effort to clarify the mechanism whereby desaturation occurs in individuals with sickle-cell anemia and its variants. In addition, observations were made on the hemodynamic alterations accompanying cardiomegaly in these states and on the relationship of intravascular oxygen tension and degree of sickling to the sickle-cell crisis. Unsaturation of the arterial blood was demonstrated in 16 of 21 patients possessing S-type hemoglobin in various combinations. By measuring A-a gradients on 3 levels of oxygenation, it was determined that desaturation is principally the result of intrapulmonary shunting of blood, although defects in diffusion also exist. Increased cardiac outputs and blood volumes were accompanied by generally decreased pulmonary vascular resistances, suggesting that cor pulmonale is not common in these states. The administration of low concentrations of oxygen (9 to 11%), while producing increased sickling in both the arterial and the venous circulation, resulted in no discernible acute or chronic symptoms.

Triiodothyronine: Clinical Effects in Patients with Suboptimal Response to Other Thyroid Preparations. S. Newman and R. F. Escamilla. California Med. **88**:206-210 (March) 1958 [San Francisco].

Over a period of 2 years, Trionine (DL-triiodothyronine) and Cytomel (L-triiodothyronine) were administered to 30 patients. Twenty-six of the patients were females and 4 were males. The age range was from 14 to 64 years. All but 3 patients had taken thyroid preparations for more than 1 year in daily doses ranging from 0.12 to 0.55 Gm. (2 to 8 grains) of desiccated thyroid or equivalent. Twenty-four had taken more than 0.2 Gm. (3 grains) a day for more than a year, and those taking less were unable to tolerate an increase in dosage. However, all continued to have symptoms, physical findings, or laboratory results suggesting persistent hypometabolism or significant side-effects that prevented further increase in dosage of thyroid preparations. Whenever possible, a dose of triiodothyronine at least equivalent to the previously administered dose of thyroid was given, so that the effects could be compared. For this study, Trionine was supplied in tablets of 50 mcg. (later labeled 25 mcg. according to content of L-triiodothyronine), and Cytomel in tablets of 5 and 25 mcg. Some of the patients received Trionine and Cytomel at different times, and others were given a combination

The place of publication of the periodicals appears in brackets preceding each abstract.

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of 1 of the triiodothyronine preparations along with thyroxin or desiccated thyroid. Triiodothyronine was withdrawn in 1 patient after a few days because of side-effects. Three patients were treated for 1 month, and the remainder for 2 months or more before the therapeutic effect was evaluated. Eight patients were treated with triiodothyronine for at least 6 months, and 2 for more than 1 year.

The condition of 13 patients was improved and that of 17 was unimproved or became worse. Side-effects occurred in 9 of 34 trials and could not always be eliminated by decreasing the dosage. The highest percentage of good response occurred in a small group (4 of 5) who received a combination of desiccated thyroid or thyroxin with supplemental triiodothyronine. Despite careful analysis of the data, no basis was found on which to predict which patients would receive benefit from the triiodothyronine. However, the occasional improvement, sometimes dramatic, suggested that a therapeutic trial with triiodothyronine in difficult or unresponsive cases of hypometabolism or hypothyroidism is justified.

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Idiopathic Renal Glycosuria in Three Generations with High Incidence. E. Gjone. Nord. med. **59**:306-307 (Feb. 20) 1958 (In Norwegian) [Stockholm].

In the family studied, a man in the first generation and his 4 children and 2 of the 5 siblings in the third generation have renal glycosuria, and a third probably also has a low renal threshold. None have symptoms of diabetes mellitus or blood sugar curves which might point toward diabetes mellitus. Renal glycosuria is usually an asymptomatic condition. In some cases there may be fatigue or lack of tone, and glycosuria as such may give local symptoms due to genitoanal infections. Apart from therapy directed to the local symptoms, the condition does not require treatment. Diagnosis is important for the patients, so that they may know that neither change in the way of life nor dietetic measures are necessary; they will also know that they do not have any form of diabetes mellitus and are not more predisposed than other persons to develop this disease.

Circulatory Changes in Chronic Liver Disease. J. F. Murray, A. M. Dawson and S. Sherlock. Am. J. Med. **24**:358-367 (March) 1958 [New York].

The authors studied the circulatory changes in 24 patients with chronic portal cirrhosis, in 6 patients with chronic biliary cirrhosis, and in 6 patients with extrahepatic portal vein obstruction and compared the findings in these 36 patients with those in 14 normal persons. Twelve of the 24 patients with portal cirrhosis had a cardiac index above the upper limit of normal. Clinically, these patients had evidence of increased peripheral blood flow and ejection systolic murmurs. Roentgenographic or electrocardiographic changes were uncommon. Patients with biliary cirrhosis and portal vein obstruction had normal cardiac indexes. An increased total blood volume, mainly plasma volume, was found in patients with portal cirrhosis who had an increased cardiac index, a large portal-systemic collateral circulation, arterial oxygen desaturation and low serum albumin levels. The increased portal venous network did not account for the increased blood volume in portal cirrhosis, as patients with extrahepatic portal vein obstruction had virtually normal blood volumes. The low serum albumin levels may, in part, represent the dilution of a normal amount of circulating albumin by an increased plasma volume. Four of the 24 patients with portal cirrhosis had low arterial oxygen saturation. Cardiac catheterization data in 1 patient and pulmonary function studies in 2 others suggested that the arterial desaturation may have been due to the shunting of blood through pulmonary arteriovenous anastomoses. The case of 1 of these patients is presented in detail.

In most patients with portal cirrhosis the increased cardiac output was tolerated without evidence of decompensation. Congestive heart failure was present in 1 patient reported on in detail. As liver functions and the clinical status of patients with portal cirrhosis improved, the cardiac output returned to normal. The mechanism of production of the hyperdynamic circulatory state in portal cirrhosis is unknown. There is profound vasodilatation, and the mechanism of this is discussed. No specific therapy is indicated for patients with a hyperdynamic circulation unless decompensation is present. Therapy should be directed to improving the underlying liver disease.

Muscular Dystrophy: Evaluation of Adrenal Cortical Function and Influence of Corticotropin, Cortisone and Testosterone. L. J. Soffer, J. Geller and J. L. Gabrilove. Metabolism **7**:97-107 (March) 1958 [New York].

Three women, between the ages of 50 and 55 years, with dystrophia myotonica and 1 35-year-old man with progressive muscular dystrophy of the facioscapulohumeral type were studied by the authors in an attempt to ascertain the status of adrenal cortical function in patients with muscular dystrophy of both the progressive and the myotonic type. The authors also wished to investigate the influence of corticotropin, cortisone, and testosterone on such biochemical parameters as creatine and creatinine excretion, serum and urine amino acid levels, organic phosphate excretion, folic acid

and vitamin B_{12} metabolism in patients with this disorder and to observe the clinical effect of hormone therapy. Two of the women with dystrophia myotonica and the male patient with the facioscapulohumeral form of dystrophy were given corticotropin for short periods in either the lyophilized aqueous form or as a repository corticotropin (ACTH) preparation. The same 3 patients were subsequently given cortisone orally. The duration of treatment varied from 4 to 16 months. The third woman with dystrophia myotonica received testosterone propionate and testosterone enanthate in sesame oil (Delatestryl) by intramuscular injection for 4 months. All the patients, with the exception of the third woman, received in addition 40 Gm. of gelatin administered orally daily.

The 2 patients with dystrophia myotonica treated with adrenal steroids and corticotropin showed striking improvement in the myotonia and subjective well-being, gaining 20 to 33 lb. in weight, and were able to engage in muscular activities previously impossible. The patient with dystrophia myotonica who was given testosterone showed little change objectively and subjectively. The patient with facioscapulohumeral dystrophy treated with cortisone remained unchanged.

No uniformity was observed in the results of the adrenal cortical function studies in the patients with dystrophia myotonica. In 1 woman, the changes obtained in the 24-hour urinary excretion of the neutral 17-ketosteroids and formaldehydogenic corticoids and in the plasma 17-hydroxycorticoids after stimulation with corticotropin indicated impaired adrenal function. The second woman with dystrophia myotonica revealed an inadequate adrenal cortical response to the intramuscular administration of corticotropin, as measured by the 24-hour urinary excretion of the neutral 17-ketosteroids. The urinary and plasma glycogenic corticoid responses to the administration of corticotropin were adequate in this patient. It may be concluded that some abnormalities in adrenal cortical function existed in both these patients. Adrenal function was normal in the third woman with dystrophia myotonica and in the man with facioscapulohumeral dystrophy. Corticotropin, cortisone, and testosterone did not influence creatine tolerance in any of the 4 patients. The urinary organic phosphate excretion was reduced in all patients given corticotropin and cortisone. In the 1 patient treated with testosterone, there was no change in the urinary excretion of organic phosphate. No conclusions concerning the effect of corticotropin, cortisone, or testosterone on amino acid tolerance could be drawn from the authors' studies. The vitamin B_{12} and folic acid blood levels were normal in all patients and remained uninfluenced by corticotropin therapy.

The Geographic Distribution of Coccidioides Immitis and Possible Ecologic Implications. K. T. Maddy. Arizona Med. **15**:178-188 (March) 1958 [Phoenix].

The Lower Sonoran Life Zone, one of several biological regions into which the United States have been classified, is characterized by arid and semiarid climates, with hot summers and few winter freezes, a low altitude and an alkaline soil. This limits plants and animals to certain types that can survive in this environment. It is the only environment which seems to permit Coccidioides immitis to exist in nature. Presumably the fungus grows primarily in the soil. A preliminary study of the plant and animal association within the Lower Sonoran Life Zone in relation to areas of varying endemicity for coccidioidomycosis, carried out by the author in Arizona, New Mexico, Texas, Utah, Nevada, and California, revealed a close correlation between the geographical areas of the Lower Sonoran Life Zone and the known endemic areas for coccidioidomycosis in the United States. July mean temperatures from 80 F to about 90 F, January mean temperatures from 39 F to 53 F, and an annual rainfall of about 5 to 20 in. seem to be the most ideal for the propagation of C. immitis in nature. The parts of the Lower Sonoran Life Zone with a more or less arid climate or with lower summer mean temperatures are apparently less favorable areas for the fungus to propagate. Thus, some areas of the Lower Sonoran Life Zone that had not been delineated as endemic areas for coccidioidomycosis are now so designated by the author who carried out coccidioidin tests on home-raised cattle in these areas. Other areas in which C. immitis infections could be expected to occur have also been designated.

Patient Accidents Occurring in Hospitals: Epidemiologic Study of 614 Accidents. H. M. Parrish and T. P. Weil. New York J. Med. **58**:838-846 (March 15) 1958 [New York].

The authors investigated all accidents occurring among the inpatients at the Mount Sinai Hospital in New York City (a large general hospital) during one calendar year. The accident report forms of the hospital were used for this investigation. There were 614 accidents among 23,911 admissions during the year studied, an annual incidence of 25.7 per 1,000 patients. [In addition, the authors estimated that between 300,000 and 550,000 patient accidents occur each year in American hospitals.] The accident rates were more than twice as high among male patients as among female patients. The rate among ward patients was 42.5 per 1,000 as compared with a rate of 17.3 for semiprivate and 13.5 for private patients. Accidents per 10,000 days of patient exposure were found high among the very young, under 1 to 9 years of age, and

among adults, aged 40 to 79. Fortunately, approximately 45% of patient accidents resulted in no detectable injury, and less than 5% resulted in a serious injury or death. With the exceptions of falls from bed and falls in the bathroom, all types of accidents occurred more frequently during the hours from 6 a. m. to 6 p. m. Approximately 70% of all accidents occurred within a 10-ft. radius of the patient's bed. Faulty physical equipment and hospital personnel played contributing roles in less than 10% of the accidents.

Falls from bed were the most frequent type of accident and accounted for 283 (46%) of all accidents. Of 283 falls from bed, 106 happened while bedrails were in place. In the opinion of these authors, beds and side-rails now in use are not designed for safety. Most beds are too high for a patient to get in and out of bed without risking a fall and subsequent injury. Bedrails are ineffective in keeping many irrational and restless patients confined to bed. The authors believe that safely designed beds and effective side-rails or restraints would reduce both the frequency and the severity of bedside accidents. Defects in the patient's mental, emotional, and physical status were prominent among the causative factors for accidents and were difficult to control. Only about 50% of the patients were completely alert and rational at the time of the accident. Patients with defects of their neuromuscular or skeletal systems and those with advanced cancer and heart disease were especially susceptible to accidents. Patients who have received sedatives, narcotics, or anesthetics require special care. Rubber airways are preferable to metal ones. Many accidents involving wheel chairs and crutches could have been prevented by instructing patients on how to use them properly. Personnel should assist elderly, crippled, and senile patients to the bathroom and to bed. What is needed is a team approach, one in which a hospital administrator, a physician, a nurse, an epidemiologist, a safety engineer, and a biostatistician coordinate their efforts. Patient accidents conform to a definite epidemiologic pattern. They can be prevented in many instances.

Universal Edema After Diabetic Precoma Treated with Thiamine. T. Deckert. Ugesk. læger **120**:224-226 (Feb. 13) 1958 (In Danish) [Copenhagen].

From the 4th to the 14th day after treatment for diabetic precoma a woman, aged 24 years, developed universal massive edema, with weight increase of 18 kg. (39.6 lb.). There were no signs of cardiac, renal, or hepatic disease; no disturbance of the electrolyte balance was demonstrable. On intensive thiamine therapy the edema disappeared in 7 days, with loss of 13 kg. (28.6 lb.) in weight. Thiamine deficiency is thought to have been the essential cause of the edema.

SURGERY

Grave Cerebral Fat Embolism: Treatment and Prognosis. P. Heimann. Nord. med. **59**:260-262 (Feb. 13) 1958 (In Swedish) [Stockholm].

Two cases of massive fat embolism are described. The first patient was admitted with fractures of the right thigh and right upper arm and facial injuries; the second, with fractures of the left leg and thigh and right upper arm. Both patients had marked symptoms in the pulmonary circulation and in the cerebral vascular system. The clinical picture was alarming. The patients were successfully treated with chlorpromazine in large doses (400 mg. intramuscularly administered daily). Antibiotic treatment, exact fluid balance, and in one case tracheotomy were features of the intensive treatment during the acute phase. Later, open reduction of the fractures was accomplished. No side-effects followed the administration of chlorpromazine. On follow-up no remaining symptoms from the cerebral fat embolism were demonstrable. There seem to be no late cerebral complications even after massive fat embolism. After 4 to 6 months the patients showed no signs of cerebral damage or other neurological symptoms.

Chemopallidectomy and Chemothalamectomy for Parkinsonism. I. S. Cooper, G. J. Bravo, M. Riklan and others. Geriatrics **13**:127-147 (March) 1958 [Minneapolis].

The authors performed operations on the basal ganglions in 600 selected patients with Parkinsonism. Twenty-one per cent of the patients had serious psychological abnormalities, 5% had latent schizophrenia, and 14% showed signs of organic mental disease. Fifty of the patients were subjected to occlusion of the anterior choroidal artery. In 550 patients destructive lesions of the globus pallidus or the ventrolateral nucleus of the thalamus were produced by the injection of a neurolytic agent, either dehydrated alcohol or an 8% solution of a specially prepared cellulose in 95% ethyl alcohol (Etopalin). Five hundred consecutive patients with Parkinsonism, who for various reasons were not operated on, served as a reference group.

Favorable results were obtained with occlusion of the anterior choroidal artery in 35 of the 50 patients with far-advanced and incapacitating Parkinsonism. In many patients both tremor and rigidity as well as long-standing postural deformities were completely abolished. These patients were followed closely for 5 years without recurrence. Favorable results were obtained in somewhat more than 70% of the 550 patients treated by chemopallidectomy and chemothalamectomy. There was objective alleviation of tremor, rigidity, and incapacitation without infliction of any neurological deficit. In

certain patients there has also been improvement in masked facies, elevation of mood, decrease in greasiness of the skin, and, in rare instances, mitigation in oculogyric crises. The mortality rate in the 600 patients was 3%, with a 2% incidence of hemiplegia. About 10% of the patients showed signs of involvement of the pyramidal pathways in a transitory form, but these signs abated somewhat within 3 to 6 weeks after the operation. About 20% of the patients with operation on the dominant hemisphere of the brain had transitory speech difficulties during the acute postoperative period, but lasting aphasia was produced only in 2. Most speech difficulties have been related to placement of the trephine opening too far posteriorly. When operating on the dominant side of the brain, the bur hole should be placed anterior to the coronal suture.

Because of the extremely variable and protean symptoms of Parkinsonism, one must select patients only after painstaking evaluation. The ideal candidate for surgical intervention is one who has unilateral tremor and rigidity. Bilateral Parkinsonism can be treated by performing the surgical intervention on the basal ganglions first on 1 side and at least 6 months later on the other side of the brain. In patients of advanced age it is deemed advisable to operate only on 1 side, even though the patient may have bilateral symptoms. In the early stages of the authors' investigation, occlusion of the anterior choroidal artery was confined to totally incapacitated patients, but as techniques became more certain and the risks became minimal, it became possible and desirable to perform chemopallidectomy and chemothalamectomy on patients in an earlier stage of the disease. With the introduction of a brain needle or cannula with 2 lumens through a small trephine opening in the skull under roentgenographic control provided by iophendylate (Pantopaque) combined with the neurolytic agent, and with a small inflatable balloon at the extremity of the cannula, to which 1 of the lumens leads, it is possible to produce an accurately localized lesion and to perform a physiological test by balloon inflation in the globus pallidus or thalamus in the conscious, cooperative patient. Thus, the result can be predicted before infliction of a permanent lesion. The indwelling brain-cannula technique allows the surgeon to tailor the size of the lesion to the needs of a particular patient. Contraindications to surgery are as follows: organic mental deterioration, psychosis, or pseudobulbar palsy with inability to swallow or speak; excessive vegetative symptoms, such as hyperpyrexia, hypersalivation, and flushing of the skin; physiological old age with marked evidence of arteriosclerosis in a patient who appears much older than his stated age; and ordinary medical contraindications, such as cardiac or renal failure or extreme hypertension.

Intravenous Cholangiography in Detection of Stone-bearing Cystic-Duct Remnants (So-called Re-formed Gallbladders). J. E. Berk and R. N. Lee. Am. J. Digest. Dis. **3**:220-228 (March) 1958 [New York].

The authors report on 6 women, between the ages of 38 and 68 years, who had undergone cholecystectomy for severe epigastric pain, who began to have symptoms similar to those experienced before the cholecystectomy, and in whom a stone-bearing dilated cystic-duct remnant or so-called re-formed gallbladder was revealed by intravenous cholangiography. These 6 cases of stone-bearing re-formed gallbladder were detected among routinely performed intravenous cholecystocholangiographic studies at the Sinai Hospital in Detroit within a period of 22 months. These observations suggest that stone-bearing cystic-duct remnants occur more often than has been generally appreciated; they also emphasize the need to explore the biliary ducts diligently for calculi at the primary cholecystectomy and to remove the entire gallbladder and as much of the cystic duct as possible.

Indications to Radical Surgical Intervention in Patients with Carotid Body Tumors. M. Wenzl. Klin. Med. **13**:49-53 (Feb.) 1958 (In German) [Vienna].

The author reports on a 40-year-old woman with a carotid body tumor on the right side of the neck, which had been growing slowly for 13 years until acceleration of growth was causing considerable difficulty in breathing and a disturbing throbbing in the neck and ear. Surgical intervention revealed a tumor which was sharply limited by a capsule and which surrounded the carotid bifurcation so intimately that its removal seemed to be possible only with simultaneous resection of the vessel. Both the external and the internal carotid arteries were almost completely compressed by the tumor. Compression of the common carotid artery for 20 minutes did not cause any symptoms, and extirpation of the tumor was decided on. Microscopic examination of the operative specimen revealed a paraganglioma. Three days after the operation hemiplegia occurred on the left side, but improvement resulted rapidly from various vasodilator procedures and repeated stellate ganglion blockade. Complete return to health resulted from further after-treatment at a hospital for nervous diseases.

The risk of the resection of the carotid bifurcation which was passing through the tumor seemed to be less severe, since the slowly progressing compression of the blood flow in the internal carotid artery suggested an accommodation of the brain to the reduced blood perfusion. This seemed to warrant effective protection against cerebral complications. Despite the relatively favorable cir-

cumstances, the reported case has clearly shown that neither the compression of the common carotid artery carried out in the course of the operation without causing symptoms nor the compression of the carotid bifurcation by the tumor itself may prevent with certainty the occurrence of temporary cerebral complications. The author, therefore, advises against an aggressive surgical intervention on carotid body tumor, since these tumors are nearly always benign, show a slow growth, and are causing relatively few symptoms. Only increasing complaints caused by displacement of adjacent organs justify surgical intervention. Radical extirpation of the tumor with simultaneous resection of the carotid bifurcation is associated with an enormous risk and should, therefore, be performed only in exceptional cases in which, besides the rapidly accelerated growth of the tumor and corresponding clinical symptoms, adequate cerebral circulation has been assured by the compression of the vessels depending on the tumor or by restoration of the circulation with the aid of anastomosis of the vascular stumps of the carotid artery. Definite proof of malignant degeneration is of only theoretical significance as an indication to radical surgical intervention because of the rarity of such an occurrence.

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Indications and Results of Ligation of the Internal Mammary Arteries in the Treatment of Coronary Insufficiency. G. Gucci. Riforma med. **71**:1438-1441 (Dec. 14) 1957 (In Italian) [Naples].

The author advocates ligation of the internal mammary arteries as a prophylactic measure in the management of mild subacute or chronic coronary insufficiency to anticipate the grave form of the disease. Originally this procedure was employed for treatment of an infarct of the myocardium and of angina pectoris. Twelve patients with mild coronary insufficiency were operated on by performing 24 ligations during the last year. Disappearance of anginal pain was noted in all patients. The relief indicated that a revascularization process had taken place. Schellong's test for circulatory function showed improvement in all patients. Electrocardiographic findings also showed tendency toward normalization of circulation in many patients. Signs of preceding infarctions remained unchanged. The postoperative course was uneventful, and no recurrence developed.

Ligation of the internal mammary arteries for treatment of coronary insufficiency may not be used as a procedure of urgency or after chemotherapeutic measures have been exhausted, but rather as an adjunct to other therapeutic procedures for treatment of coronary sclerosis. There are few contraindications to this operation, and they are related to the cardiac, rather than to the general, state of health. The best time for this operation is 5 to 6 months after an infarction, when the lesion has cicatrized and the hemodynamic function has stabilized.

Aneurysm of the Abdominal Aorta. K. N. Morris. Australian & New Zealand J. Surg. **27**:183-192 (Feb.) 1958 [Melbourne].

Morris discusses the clinical aspects and the management of aneurysm of the abdominal aorta, pointing out that rupture of the aneurysm is a common terminal event and that operation should be undertaken, if possible, before rupture occurs. In 15 of the 24 patients observed by the author, the aneurysm had already ruptured. Among the 9 patients in whom the aneurysm had not yet ruptured, there were 2 who did not have any symptoms. One of these was an 82-year-old woman, and the other was a man in poor general condition. In both of these instances operation was not recommended. There were only 2 patients who were classed as "good risks." One had mild symptoms, and the other had pain suggestive of impending rupture. Operation was undertaken in both of these. The first patient did well; the second died of a coronary occlusion 6 days after operation. The remaining 5 patients were all in the "bad-risk" category for such reasons as angina pectoris, severe hypertension, auricular fibrillation, and cardiac failure. These patients were subjected to operation because of intolerable pain or threatened rupture. Two died, and 3 survived.

Of the 15 patients on whom operation was performed after rupture, 6 are now alive after periods varying from 5 to 30 months. It is difficult to imagine a group of patients who would constitute a worse operative risk than this. The salvage rate is low, but, in view of the almost certain fatal outcome if untreated, even this low rate is worthwhile. The causes of death were mainly related to the patient's age, the condition of his cardiovascular system, and his kidneys. It cannot be anticipated that operations of this magnitude, carried out on this type of patient, can ever be uniformly successful. The author comments on various operations for aneurysms of the abdominal aorta. The tabulations of his own cases show that he used a nylon prosthesis, particularly in the operations that were performed prior to rupture but also in some of those performed after rupture. Homograft replacement and reconstruction of the aorta from the wall of the aneurysm were employed in other patients.

A Clinical Trial of Prednisolone in Bone and Joint Tuberculosis. A. J. M. Cathro. East African M. J. **35**:31-35 (Jan.) 1958 [Nairobi, Kenya].

The idea behind the present investigation was to administer prednisolone along with antituberculous drugs in cases of bone and joint tuberculosis in the hope that this therapy would enhance the effect

of the antibiotics by removing and inhibiting the formation of fibrous tissue. It seemed possible that such a regimen might facilitate operations on the affected joints or even do away with the need for radical surgery altogether. Sixteen patients with active tuberculosis of bone and joint were chosen at random. Their ages ranged from 4 to 47 years, the average age being 16 years. Ten patients were given prednisolone, and 6 served as controls. In the test series, after the diagnosis and a clinical evaluation had been made, antituberculous therapy in the form of streptomycin and isoniazid was begun. After an interval of 1 to 2 months, depending on the progress, prednisolone was given for 2 months, chemotherapy being continued meanwhile. In view of the danger of delayed wound healing, surgery was postponed in those patients requiring it for 1 to 2 months after the withdrawal of prednisolone. In the control series the patients were observed over a corresponding period of time under the influence of streptomycin and isoniazid alone. Antituberculous therapy was maintained in the usual way after treatment with prednisolone and in both series after surgery.

The daily doses for adults were 1 Gm. of streptomycin, 0.6 Gm. of isoniazid, and 20 mg. of prednisolone, the last 2 treatments being given in divided doses. Children were given proportionately smaller doses. Of the 10 patients treated with prednisolone, 7 had tuberculosis of the spine, 6 in the lumbar region and 1 in the thoracic region; 2 had tuberculosis of the knee joint; and 1 had tuberculosis of the hip joint. In the group with spinal disease, 2 patients had an active pulmonary lesion as well, 1 had chronic tuberculous arthritis of the right carpus, and 1 had paraplegia of a year's duration. One patient with tuberculous arthritis of the knee had a calcified pulmonary lesion. The limited number of patients does not permit a definite opinion on the effect of prednisolone. The findings at operation disproved the idea that prednisolone is a solvent of pathological fibrous tissue. Prednisolone did not prevent bone absorption or sequestration. It may have been a factor in speeding up new bone formation in some of the patients observed. There would appear to be no contraindication to the use of prednisolone in active tuberculosis or osteoporosis, as is commonly stated. There is no conclusive evidence that prednisolone facilitates or obviates surgical intervention in bone and joint tuberculosis.

Biliary Tract Surgery in Retrospect. A. Cass, K. Glass and J. Smith. Australian & New Zealand J. Surg. 27:193-203 (Feb.) 1958 [Melbourne].

The first part of this discussion is concerned with certain aspects of the operations for calculi of the biliary tract performed on 180 patients. Twenty-two (12%) of the operations were for acute complications. The authors differentiate between "acute compulsory" (rupture of the gallbladder) and "acute elective" cases. No "acute elective" operations were done until it was seen that the over-all mortality in the first 100 operations was 1%. Most of the operations for acute conditions were, therefore, among the last 80 patients. No elevation of the mortality rate occurred. During this period occasional patients with acute complications have not been subjected to immediate surgery if superadded conditions, such as congestive cardiac failure, were present. The cholecystostomies were performed on patients with ruptured gallbladders whose condition was so parlous that the anesthetist demanded speed. The choledochostomy rate was 35%; stones were found in 60% of the ducts opened. This means that in 22% of all the patients in this series 1 or more stones were found in the common bile duct. The addition of choledochostomy to cholecystectomy did not elevate the mortality rate. Choledochostomy is required so frequently in biliary tract surgery that there is no place for the cholecystectomist who rarely, if ever, performs it. The removal of all stones in the bile ducts (Lahey's "third stage") has not yet been achieved. The percentage of patients having stones in their common bile ducts at operation is obviously bound up with the range of the indications for biliary tract surgery. If these indications are extended to include (for example) noncalculous cholecystitis, then a lower percentage of common bile duct stones is likely.

The second part of this paper is concerned with a follow-up study of 951 patients, which revealed that there are trustworthy indications for biliary surgery, less trustworthy ones, and some common mistakes. The trustworthy indications are biliary colic, obstructive jaundice, and acute cholecystitis. The less trustworthy ones are dyspepsia (because 2 in 3 cases recur), a "positive" Graham test, incidental stones (e. g., found at laparotomy), and the fear of cancer. The common errors are peptic ulcer and operating for pains which are not biliary colic (e. g., due to spondylitis). Biliary colic, jaundice, and dyspepsia were studied during the follow-up. The authors also evaluated the likelihood of the development of cancer or of symptoms in those with symptomless gallstones. It was found that undue reliance on Graham's test can result in a cholecystectomy being performed when the only lesion present is a peptic ulcer. This survey showed that the postcholecystectomy syndrome is a confusing concept. Ideas on postcholecystectomy syndromes are determined by what surgeons expect of the operation. For example, the gallbladder may be removed because the patient has biliary colic plus dyspepsia, and the dyspepsia persists after the operation. The authors disagree with certain views expressed by American surgeons. They regard as doubtful the following statements: (1) "Calculous cholecystitis, whether symptomless or not, is an indication for remedial surgery"; (2) "gallbladder

disease should be eradicated before patients reach old age and develop complications, such as jaundice, acute inflammation, or malignancy"; and (3) "they ['the silent gallstones'] should be removed before the shriek of malignancy." The survey suggests that not only is this language extravagant but the ideas behind it are also.

The Treatment of Acute and Chronic Ulcerative Colitis. C. H. Brown. Am. Pract. & Digest Treat. 9:405-411 (March) 1958 [Philadelphia].

The author reports his experience with the management of patients who had nonspecific, idiopathic, ulcerative colitis. The exact number of patients who were treated medically is not given. Twelve patients were given steroids for relatively short periods of time (10 to 30 days). Surgical treatment was given to 211 patients. The 2 basic fundamentals of medical treatment are rest and food. Rest should include complete mental, emotional, and physical relaxation. A high-protein, high-carbohydrate, high-caloric, and low-residue diet is imperative. If the patients is unable to eat, parenterally administered fluids must be given. It frequently is difficult to give the required daily amount of 3,500 calories parenterally, and, therefore, a continuous drip of eggnog, amino acids, and protein and carbohydrate supplements may be administered with the aid of a stomach tube. If the patient is able to eat, his daily diet is increased to 3,500 calories with 150 Gm. of protein. Stimulation of the appetite with small doses of insulin before meals may help. Antispasmodics, such as atropine and belladonna, can be given to rest the colon. The potent anticholinergic drugs, such as methscopolamine (Pamine), propantheline (Pro-Banthine), and diphemanil (Prantal), are more effective in decreasing gastrointestinal motility. The most important supportive measure is the transfusion of whole blood. Supplemental vitamins administered in rather large doses are necessary and should include vitamins A, D, C, and the entire vitamin B complex. The administration of minerals and electrolytes, such as calcium, iron, sodium, chlorides, and potassium, may be necessary in severely ill patients. Oxytetracycline (Terramycin), given in doses of 250 to 500 mg. 4 times daily, and the other antibiotics may be of help in controlling secondary infection. The nonabsorbable sulfonamide preparations, phthalylsulfathiazole (Sulfathalidine) and succinylsulfathiazole (Sulfasuxidine), are of particular value in ulcerative colitis, and tablets of 2.5 Gm. 4 times daily may be given for long periods of time. Eighty-seven per cent of the patients with ulcerative colitis made satisfactory progress on this medical program.

The author's experience with steroid therapy was not sufficiently favorable to warrant the routine use of steroids in the treatment of ulcerative colitis. Although in the course of this therapy the temperature returns to normal, the patient feels more comfortable, and the appetite improves, the proctoscopic appearance of the rectal mucosa remains the same, the diarrhea usually is unaltered, and, when the drug is withdrawn, the fever frequently returns. Steroid therapy for ulcerative colitis should be used only in selected patients. Twenty units of corticotropin (ACTH) may be given intravenously daily when steroid therapy is instituted. This may be switched to Acthar Gel, 80 units administered intramuscularly daily, and subsequently to prednisone or prednisolone, 15 to 30 mg. given by mouth daily.

In 60 of 106 patients subjected to surgical treatment up to 1949, the results were excellent; 17 of the 60 patients had ileostomy alone, 32 had colectomy after preliminary ileostomy, and 11 had other surgical procedures. Ten obtained reasonably satisfactory results, 11 were therapeutic failures, 8 were lost to follow-up, and 17 died within 2 months after the operation. Surgical treatment is indicated only for those patients who continue to be acutely or chronically ill despite an intensive trial on adequate medical treatment. Ileostomy alone seldom arrests the disease and is attended with a mortality rate of 23%. When surgical treatment is necessary, subtotal colectomy and ileostomy in one stage is a safe procedure associated with a low mortality and low morbidity and is the operation of choice. It was performed on 105 patients who were operated on between 1949 and 1957; only 4 of these patients died in the hospital, and 1 died after his discharge from the hospital.

Recurrent and Persistent Varicose Veins. H. Dodd. Postgrad. M. J. 34:73-76 (Feb.) 1958 [London].

Follow-up studies on more than 1,000 patients from 3 to 10 years after operations for varicose veins revealed that the author had obtained good results in 90% of the patients. Yet in the period from January, 1952, to June, 1957, over 400 procedures had to be performed for varicose veins that had recurred or persisted after operation. These patients returned with complaints of prominent veins, itching, pain, swelling, eczema, or ulceration of the leg. These conditions were caused by several factors, either singly or in combination: 1. The diagnosis was incorrect or incomplete. 2. The operation was wrong or inadequate. 3. New varices had developed. 4. Follow-up care was omitted. After discussing these 4 points, the author shows that the treatment of persistent or recurrent varicose veins is the same as that of the primary varicose veins. The sites of high-pressure leak or leaks from the deep veins into the superficial veins are exposed beneath the deep fascia, and the vessels are divided, if possible, flush at their entrance into the main vein. There are 5 common leaks of venous hyper-

tension, and experience shows that several may coexist, although 1 or 2 are the usual finding. The saphenofemoral and saphenopopliteal junctions are the most common, and then follow the incompetent communicating veins above the ankle. There are the communicating veins passing into the femoral vein at Hunter's canal and into the popliteal vein around the knee joint. Defective veins perforating the tensor fasciae femoris and the hamstring muscles are comparatively rare.

Describing the operation for persistent varicosities of the long saphenous veins, the author says that an operation in the groin or popliteal space in the presence of the varicocele-like masses of thin-walled veins and scar tissue which develop after inadequate ligation may require 1 to 1½ hours. The principle followed is that of approaching the femoral or popliteal veins through virgin tissue and working up or down until the saphenofemoral or saphenopopliteal junctions are found. These are transfixed with fine thread and divided. Then the faulty saphenous trunk is exposed at the ankle, the stripper is passed along it, and the trunk is stripped out. Operations for persistent or recurrent varices at other sites are also briefly described. Full diagnosis and adequate operations of recurrent varicose veins are exacting but satisfying. Many persons, who are otherwise well, are incapacitated by varicose veins, the commonest surgical condition. Most persons, including the aged, can be materially improved, if not cured, by good treatment.

General Principles of Fracture Management in the Aged. E. D. Bick. Surg. Gynec. & Obst. **106**:343-346 (March) 1958 [Chicago].

A series of more than 500 fractures and dislocations occurring among the elderly was studied. Tabulation of data on 516 persons, over the age of 60 years, who sustained fracture and dislocations shows that, with 3 exceptions, the distribution is more or less the same as would be found in any group of adults. The exceptions are the hip, the vertebra, and the shoulder, which together represent 58% of the total. Fractures about the wrist, which are third in numerical order, would be equally high or higher in any general list. These represent another 14%. The 3 exceptions also represent temporary total disabilities, and 2 of them, the hip and the vertebra, often represent permanent partial disabilities of significant degree. Fractures occur more frequently in women than in men. In those between the ages of 60 and 75 years the ratio of females to males is 3 to 1; in individuals more than 75 years old the ratio is 11 to 1. The aged population of New York in 1956 showed an over-all ratio of 1.2 females to 1 male. One must therefore assume that elderly women are far more subject to fracture than are their male contemporaries.

There are no techniques especially applicable to the treatment of fractures of the aged, but there are limitations of objectives. First, there is a greater need for a resting period between emergency care and definitive treatment. Manipulation or surgery is best performed after the patient has been allowed time for recovery from the shock of trauma. A second limitation is the relative softness or compressibility of the bones. Aging bone will not withstand the internal pressures of screws, plates, or nails as readily as does more viable bone. This is, of course, a variable factor and does not necessarily contraindicate the use of internal fixation. However, such procedures are less dependable in the aged. A third limitation appears during the period of after-care. There is the normally decreased elasticity of the muscular and periarticular connective tissues. It implies easy postfracture strain of inelastic ligaments, capsules, and fascial planes. It becomes necessary, therefore, to temper the urge for early and rapid mobilization of the part by measures which to the tissues of an elderly person may cause excessive stretch. Enthusiastic attempts at exercise or self-stretching of the area may result in a pain-spasm sequence which retards rather than enhances mobility.

Recovery of reasonable mobility in shoulder fractures takes a much longer time than is generally anticipated. Attempts to accelerate the process by active exercise not only are apt to retard motion but also cause an unnecessary persistence of pain. In dealing with fractures of the vertebrae, graded daily walks are apt to be more salubrious than exercises directed to the muscles of the trunk. The demand of early "out of bed" is, of course, incontrovertible when its purpose is gained. However, too often the order is obeyed to the patient's actual detriment. To be lifted out of the freedom of a roomy and adjustable hospital bed and then to be immobilized in a sitting position by the cautious blanketing of a solicitous attendant who fears more the pneumonia of a draft than the hypostasis of bed is indeed a gross disservice.

PEDIATRICS

Severe Staphylococcal Infections in Young Children: The Isolation of Micrococcus Pyogenes Var. Aureus with a Specific Bacteriophage Pattern. M. L. Cooper and H. M. Keller. A. M. A. J. Dis. Child. **95**:245-252 (March) 1958 [Chicago].

During the 4th week of June, 1956, strains of coagulase-positive hemolytic Staphylococcus pyogenes var. aureus with the bacteriophage pattern 42B/44A/47C/52/80/81, apparently highly virulent for infants, were isolated from 7 patients admitted to the Children's Hospital in Cincinnati. Six of these patients were critically ill, 4 with pneumonia

and empyema, 1 with pneumonia and a large deep intramuscular abscess, and 1 with pneumonia. The 7th infant was seriously ill with a large abscess. In the course of a year a total of 77 persons, including 67 patients and 10 asymptomatic carriers, were found to harbor staphylococci with the same bacteriophage pattern. Among the 67 patients there were 60 children with skin pustules, abscesses, pneumonia, empyema, pharyngitis, bronchitis, pyarthrosis, acute otitis media, and vaginitis and 7 adults with abscesses. The 7 adult patients with abscesses included 2 nurses on the infants' ward, 2 technicians in the bacteriology laboratory, and 3 parents whose children had acute staphylococcic infections. Among the 10 asymptomatic contact carriers were 3 siblings of patients, 2 children of patients, 1 student nurse, 2 nurses' aides, and 2 physicians. In vitro sensitivity tests showed that the staphylococci were sensitive to bacitracin, chloramphenicol (Chloromycetin), erythromycin, and novobiocin; they were resistant to chlortetracycline (Aureomycin) and dihydrostreptomycin and, with few exceptions, to penicillin and tetracycline.

Three months after the first patient was admitted to the Children's Hospital nasopharyngeal cultures of 117 personnel on the infants' ward revealed that 3 were harboring coagulase-positive hemolytic Staph. pyogenes var. aureus with the bacteriophage pattern 42B/44A/47C/52/80/81. These staphylococci were readily transmitted to other members of the families of patients. A study of 14 families revealed the presence of these particular staphylococci in 27 of a total of 53 persons. In 3 of these families, all 13 members were shown to be harboring these staphylococci—in abscesses in 5, in empyema fluid in 3, and in the nasopharynx in 5 asymptomatic carriers. Of the 42 infants under 1 year of age, 28 had a common place of birth, and 25 of the 28 infants were born in May, June, or July, 1956. A survey of that institution revealed the presence of infants and mothers with pyogenic infections from which strains of Staph. pyogenes var. aureus were isolated with the bacteriophage pattern 42B/44A/47C/52/80/81. Therapy consisted of the administration of 1 or more antibiotics to which the Staphylococcus organisms were sensitive in in vitro tests. Good clinical results were usually obtained with chloramphenicol, erythromycin (Ilotycin), and novobiocin (Albamycin). There were 2 deaths among the infant patients.

Neonatal Osteomyelitis: A Disease Different from Osteomyelitis of Older Children. A. M. Clarke. M. J. Australia 1:237-239 (Feb. 22) 1958 [Sydney].

Neonatal osteomyelitis differs so much from acute hematogenous osteomyelitis of older children that it is virtually a different disease. Analyzing 24 cases that occurred during the past 5 years at the Royal Children's Hospital, Melbourne, the author found that the bones involved were as follows: femur, 8 cases; maxilla, 6; humerus, 5; vertebra, 3; clavicle, 2; ulna, 2; radius, 1; tibia, 1; talus, 1; and phalanx, 1. Several bones were involved in 3 cases, and there was 1 death from the severe pyemic type of infection. Only 3 patients had involvement of the upper end of the femur and the hip joint. The possibility of primary involvement of a vertebra is also demonstrated by 3 cases. These were not discovered until large retroperitoneal abscesses had developed. The clinical course of neonatal osteomyelitis contrasts with that of osteomyelitis in older children in that there is often little or no toxemia or pyrexia and little systemic disturbance.

Blood culture often gives negative results. Abscess formation and joint involvement are common. Sequestra are rare. A marked feature is the tremendous amount of irregularly shaped extracortical new bone formation, the extent of which is determined by the subperiosteal abscess. Bone destruction and widening of a joint space may be obvious. There are 2 different forms of the disease. In a minority of infants, in whom it is an incident in septicemia, the condition is fatal, whereas in the majority of infants, the constitutional disturbance is not great, and the condition might be called benign except for the crippling deformities which can result. Pus for culture was obtained in the majority of infants, and Staphylococcus aureus was grown on every occasion. The suggested pathogenesis is that an infected thrombus, often originating in the umbilicus, lodges in the vascular network of the metaphysis of a long bone; but as the newborn infant has little cortical bone, it, together with the cancellous bone, is soon penetrated, and pus escapes into the subperiosteal area and ruptures into the soft tissues. The periosteum in infants strips up easily, so that there is not much pus under pressure to cut off the blood supply of the shaft. Consequently, an extensive involucrum is formed, but sequestration of dead bone is uncommon. Pus escapes into the soft tissues; this saves the cortex from the destruction noticed in older children.

Whatever the local manifestation, there are often associated paronychia, skin pustules, or cord infection derived probably from 1 of the following sources: prenatal intrauterine infection; infected liquor amnii after rupture of the membranes; maternal vaginal organisms; fingers and apparatus used in cleansing the baby's mouth after birth; the mother's skin, nipples, or milk; and the skin, nose, or upper part of the respiratory tract of nurse or attendants, the last-named being by far the most important. Osteomyelitis of the maxilla is relatively common (6 cases in the present series of 24). In none of the cases was the diagnosis made before pus was exuding from sinuses inside the mouth. Usually the first sign that something is amiss is that a swelling is seen in a cheek, the infraorbital

area, or an eyelid. Exophthalmos or conjunctivitis may cause the patient to be directed first to an ophthalmologist. An alveolar swelling sometimes comes first and may proceed to perforation and discharge. Premature eruption of teeth is a characteristic phenomenon. This acceleration of eruption is probably due to increased vascularity in response to infection. Pus discharging from 1 nostril may result in an incorrect diagnosis of dacryocystitis. Successful treatment depends on early diagnosis, adequate chemotherapy, and prevention of dislocation or deformity. Early diagnosis depends on the condition's being suspected and on the appreciation of early signs, such as local edema or refusal to move a limb. In order to keep ahead of the drug-resisting characteristics of the infecting organism, the latest antibiotic should be used in adequate dosage and for sufficient time, 3 weeks being a minimum. Affected limbs should be immobilized early in their optimum position. This is of supreme importance in the hip.

Management of Nocturnal Enuresis in Childhood. S. J. McClendon. Arch. Pediat. **75**:101-105 (March) 1958 [New York].

The author treated 32 boys and 28 girls, between the ages of 8 and 14 years, for nocturnal enuresis with meprobamate. The patients were selected because of the failure of all other measures ordinarily employed in the treatment of this condition. In all patients, organic diseases and anomalies of the bladder or urinary tract had been excluded by careful history, physical examination, catheterized urine specimens, or complete urologic studies including retrograde pyelograms and cystoscopic examinations. Complete neurological examinations were done on all, including roentgenograms of the lower spine and sacrum to exclude neurological disease, spina bifida, and congenital anomalies. Instructions were given concerning voluntary bladder training, fluid restriction after 5 p. m., avoidance of harsh disciplinary measures, and electric timing devices. These measures were discussed at a conference with both parents. The child in each case was given specific instructions about these things and also was given encouragement about the final outcome of the enuresis. The initial dose of meprobamate was 400 mg. given at 6 p. m. After one week, if there had been no improvement, the dose was increased to 800 mg. given in 2 divided doses at 4 p. m. and 8 p. m. This dosage was maintained for 30 days irrespective of results. If a success was secured, the dose was reduced to 400 mg. given at 6 p. m. After 30 additional days of treatment, administration of the drug was discontinued entirely. Each patient was followed for 6 months after withdrawal of the drug. If relapse occurred, retreatment for 1 month was again advised.

Of the 60 patients, 41 obtained a complete success, 10 obtained a partial success, and 9 were therapeutic failures. Complete blood counts and routine urinalyses made every 2 weeks revealed that there were no disturbances in either category. No side-effects of the drug were noted. The use of meprobamate is not suggested as complete relief for enuresis. However, the high percentage of children who were benefited from the drug makes meprobamate in the dosage described worthy of a trial in those patients with nocturnal enuresis, who are free from bladder or kidney disease or anomalies, when all other measures of management have failed.

UROLOGY

Needle Biopsy of the Kidney. A. W. Bohne, R. C. Ackles, D. R. Drew and K. L. Urwiller. J. Urol. **79**:393-396 (March) 1958 [Baltimore].

The authors describe their technique of needle biopsy of the kidney, which they used during the last 18 months in 30 biopsies. They obtained renal tissue in 23 (76%) of the 30 patients, and they show that their results compare favorably with the results obtained by others. There were few complications. While all the patients had microscopic hematuria, gross hematuria was observed in 3 of the patients, but there was no instance of retroperitoneal hemorrhage. Complications which have been reported or anticipated included retroperitoneal hemorrhage, perforation of an intra-abdominal viscus, dissemination of a malignant or tuberculous process, or perirenal infection. The authors believe that the patient should be hospitalized for this procedure, mainly for adequate postbiopsy follow-up. It is a relatively safe procedure if done with adequate knowledge of renal position and realization of possible complications. Needle biopsy of the kidney can either correct or confirm clinical impressions.

Urological Complications of Stromal Endometriosis. C. A. Macfarlane, C. V. Hodges, H. V. Anderson and R. C. Benson. J. Urol. **79**:436-446 (March) 1958 [Baltimore].

Stromal endometriosis is a type of primary uterine neoplasm whose infiltrative growth into the parametrial areas secondarily involves other pelvic viscera. Most authors agree that the basic origin of this neoplasm is from endometrial tissue or its embryonic precursor. The one opposing concept is that of Pedowitz, who believes that this neoplasm has its origin in vascular tissue and has, therefore, classified this tumor as a hemangiopericytoma. Stromal endometriosis generally occurs during the second half of the reproductive life. The presenting complaints include those of menometrorrhagia, abnormal noncyclic uterine hemorrhage, postmeno-

pausal vaginal bleeding, pelvic pain, and lower abdominal tumefaction. The one most constant physical finding on examination is that of a symmetrically enlarged uterus. This neoplasm is distinguishable from adenomyosis and ectopic endometriosis. In the enlarged uterus diffuse infiltration of the the myometrium is evident as cord-like masses. Neoplastic growth near the endometrial surface produces an intrauterine polypoid growth in about 45% of these tumors.

With involvement of the urinary bladder, adnexa, intestine, and peritoneum, multiple firm nodules of a yellowish color are usually seen on the serosal surface. Cyst formation is not infrequent and occurs with infiltration of ovarian tissue. The tendency of stromal endometriosis to infiltrate in and along lymphatic and vascular channels has led to surgical resections that are either inadequate or deliberately palliative. The tumor residuum remaining in the parametrial areas or in the cervix after subtotal hysterectomy infiltrates the tissues and organs of the pelvis. The morbidity and mortality of stromal endometriosis are a function of involvement of anatomically vital sites rather than of neoplasm per se. Involvement of the urinary tract has been reported as approximately 12% of all cases reviewed.

In the 57-year-old woman, whose history is presented, the presenting complaints were those of an increasingly protuberant abdomen and edema of the left leg. The most striking feature on physical examination was a rounded, smooth, firm, intra-abdominal mass which extended 24 cm. above the symphysis pubis. This mass had invaded the entire pelvis, and there was a solid nodular invasion of the anterior vaginal wall. The bladder would not expand sufficiently to allow satisfactory cystoscopic examination. An exploratory laparotomy revealed that a large left ovarian cyst had 1 area of solid tumor within its wall. The peritoneal cavity itself was free of neoplastic infiltration, and there was no encroachment upon the sigmoid colon. Tumor had involved both parametrial areas with extension to, but not into, the pelvic musculature on the right. The anterior vaginal wall and vesical floor were grossly thickened. Tumor was also palpable within the dome and fundal areas of the bladder wall itself, and a yellowish subserosal nodule of tissue was present on the bladder fundus. The right ovary was replaced by a solid tumor mass. The downward course of both ureters ended in solid neoplasm with marked dilatation on the left. Anterior pelvic exenteration was performed, and urinary diversion was accomplished by means of bilateral ureteral transplants into an isolated ileal conduit with a cutaneous ileostomy. The surgical specimen weighed 715 Gm. minus the fluid contents of the ovarian cyst. Identified in the neoplastic mass were the urinary bladder, the distal portions of the ureters, urethra, a greater portion of the vagina, and both ovarian masses. This case history illustrates the usual characteristics of this disease and the surgical role of the urologist in relation to its treatment. Stress has been placed on palliative urinary diversion and curative surgical extirpation.

Malignant Pheochromocytoma with Voluntary Ability to Elevate Blood Pressure. C. L. Ransom, R. R. Landes and C. G. Gaddy. J. Urol. **79**:368-376 (March) 1958 [Baltimore].

The authors present the history of a 37-year-old man who on the day of admission to the hospital, because of a strange feeling in his chest and a sense of suffusion throughout his face when bending over or flexing himself laterally, had come directly from work to his physician. At this time, the blood pressure was 230/110 mm. Hg. When the blood pressure returned to normal, it could again be elevated at will by the patient with lateral flexion of his trunk, but direct palpation did not reproduce the phenomenon. Intravenous pyelograms demonstrated a mass lying superior to the left kidney with distortion of the renal calyceal and pelvic structures. At operation the kidney was found to be involved in a large globular mass about the size of a football. Despite generous exposure, only about the lower third of the neoplasm could be removed. The renal pedicle and the entire medial portion of the tumor appeared to be inextricably involved with the aorta and stomach in 1 amorphous mass. Since removal was impossible, the incision was closed. The patient died 14 hours after the operation as the result of a severe hemorrhage rather than of interference with the pheochromocytoma. Microscopic studies corroborated the malignant character of the pheochromocytoma, although frozen sections from the tumor capsule during the operation had been reported as neuroblastoma.

The authors cite literature on malignant pheochromocytoma, pointing out that in large series of cases of pheochromocytoma the incidence of malignancy usually ranges from 8 to 11% but that in bilateral pheochromocytomas it reaches 30%. Pressor effects, either sustained or paroxysmal, may or may not be present in malignant pheochromocytoma. The diagnosis of malignancy should be based not on cellular pathology alone but rather on evidence of invasion or metastasis. Pheochromocytomas which are diagnosed as benign may later show metastases.

Solitary Adenoma of the Kidney. F. C. Bauer Jr., D. E. Murray and E. F. Hirsch. J. Urol. **79**:377-382 (March) 1958 [Baltimore].

The authors present the history of a 65-year-old woman, who was first hospitalized in April, 1951, complaining of diffuse colicky pain in the abdomen for several months. The pain was sometimes relieved by a laxative. It became localized in the left

side of the abdomen. The patient had had loose stools for several years; mucus was present but no blood. Roentgen-ray films of the abdomen disclosed that the right kidney was not enlarged and that the left was poorly visualized. Barium enema revealed diverticula of the rectosigmoid and the distal part of the colon. No erythrocytes were found in the urinary sediment. The patient was admitted again on Sept. 4, 1956, because of (abdominal) soreness and occasional sharp pain attributed to diverticulitis of the colon. There was a diffuse tenderness of the abdomen about the umbilicus, and an indefinite mass was palpated in the region of the left kidney. Roentgen-ray films revealed a large, soft, ovoid tissue mass in the left upper quadrant, which closely approximated the kidney shadow and displaced the colon to the left. A comparison with films taken during the previous hospital stay disclosed that the soft tissue mass on the left side was present previously and had increased only slightly in size. An intravenous pyelogram demonstrated a 12-by-14-cm. mass extending from the lower pole of the left kidney. The mass had faint densities (calcium), and the lower portion of the kidney was obscured or obliterated by the mass. The inferior calyces on the left were distorted laterally and medially and appeared to override the mass.

The left kidney was removed surgically. It had a solid tumor in the lower pole without extension into the renal vein or renal fossa. Histologically, the tumor consisted of solid cords of medium-sized cells with an abundant, finely acidophilic cytoplasm and small, oval nuclei. Although most cells were uniform in size, a few were large with multilobular nuclei. The symptoms disappeared after the operation, and the patient was still well 8 months later. Adenomas of the kidney occur as a solitary tumor of an otherwise normal kidney and as single or multiple tumors of an arteriosclerotic kidney. Histologically, adenomas are papillary, alveolar, or tubular. Adenomas of the arteriosclerotic kidney frequently are papillary. Alveolar adenomas are rare. Transitions from adenoma to carcinoma (hypernephroid) have been described.

Topical Anesthesia of the Vesical Mucosa as a Tool for the Management of the Neurogenic Bladder. E. Bors. J. Urol. **79**:431-435 (March) 1958 [Baltimore].

The author studied the effect of topical anesthesia of the vesical mucosa in 124 patients with spinal cord lesions, of whom 112 had traumatic cord damage at various levels of the neuraxis below C-5, and 12 had nontraumatic diseases, such as mulitple lesions, combined degeneration, tabes, tumor, radiculitis, and partial aplasia of the sacrum. One hundred twenty-one patients had upper and 3 patients had lower motor neuron lesions. Prior to the instillation of 2 or 3 oz. of a 0.25% aqueous solution of Pontocaine, the residual urine and capacity of the bladder were determined. The Pontocaine remained in the bladder for 10 minutes and was then drained. Another residual-capacity test was done after 1 hour, and again after 24 hours. The type of voiding was observed, whether by reflex, extrinsic pressure (abdominal or manual), or a combination of both. The fluid intake was regulated by giving the patient 1 glass of water every hour during waking hours. Of a total of 124 patients, 35 responded so well to the procedure that they became catheter free; the results were good in 29 of the 112 patients with traumatic lesions and in 6 of the 12 with nontraumatic lesions. The effect of mucosal anesthesia was superior to that of sacral nerve anesthesia, which was, in turn, superior to that of pudendal anesthesia, in the 34 patients in whom all 3 methods were used.

Although the method was primarily devised for the treatment of patients with upper motor neuron lesions, it also benefited 2 patients with lower motor neuron lesions. It proved valuable in 7 of 25 patients with a preceding transurethral resection of the vesical neck, which alone did not establish bladder function. The fact that the 2 patients with lower motor neuron lesions responded favorably to topical anesthesia suggests that, in addition to the sacral mucosal reflex arcs, similar lumbar mucosal reflex arcs exist; impulses from the mucosal receptors would then be recruited by the lumbar spinal cord into an efferent outflow to the lissosphincter of the bladder. This problem needs further study, because, if correct, it would also extend the scope of the mechanism of Pontocaine action in cases with upper motor neuron lesions. Inasmuch as the sacral and lumbar afferents carry stimuli from mucosal receptors, it would seem likely that a combined relaxation of the lissosphincters and rhabdosphincters may result from this interruption of the afferent limbs of the reflex arcs. Thus, the numerically better effect which follows topical anesthesia can be understood in comparison with the other 2 methods of pudendal or sacral nerve anesthesia, which act only upon the sacral reflex arcs. Combinations of topical anesthesia with pudendal and sacral nerve anesthesia are proposed for future study.

OPHTHALMOLOGY

Lesions of the Lids: A Statistical Note. R. B. Welch and J. R. Duke. Am. J. Ophth. **45**:415-416 (March) 1958 [Chicago].

The clinical and histopathological characteristics of 617 lid lesions, their distribution with respect to sex and age, the site of predilection, and the percentages of correct clinical diagnoses were studied at the Wilmer ophthalmic pathology laboratory of the Johns Hopkins University and Hospital between Jan. 1, 1952, and Dec. 31, 1956. Three hundred

eight (50%) of these lesions were incorrectly diagnosed, illustrating the uncertainty of reliance on clinical impression alone. One hundred twenty-five (20.3%) of the 617 lesions were papillomas, 89 (14.4%) were nevi, and 80 (13%) were chalazia. Clinically, papilloma was correctly diagnosed in 70% of the cases. Seventy-four per cent of these lesions occurred in patients over 40 years of age. The occurrence of papilloma was equally divided between the sexes, and no site of predilection was manifest. Thirty-six per cent of nevi were correctly diagnosed clinically, and 80% of these lesions occurred in patients over 30 years of age. Of 85 patients with this type of lesion whose sex was known, 64 were women, suggesting a significantly higher incidence of this lesion in the female sex. No site of predilection was manifest. Chalazion was correctly diagnosed clinically in 70% of the cases; this lesion occurred with equal frequency in patients of all ages. No sex or site predilection was manifest.

Sixty-eight (11%) of the lesions were basal-cell carcinomas. This type of carcinoma occurred 8 times more frequently than either the squamous or the basosquamous carcinoma. Basal-cell carcinomas were correctly diagnosed clinically in 56% of the cases and were most often incorrectly called papillomas, nevi, recurrent chalazia, or cysts. When all types of carcinoma were grouped together, the 2 sexes were equally affected. Only 12.5% of the lesions occurred in patients less than 40 years of age. The highest incidence of occurrence (23%) was observed in patients in the 6th, 7th, and 8th decades. The lower lid was more commonly involved than either the upper lid or the canthus. Epidermoid, dermoid, epithelial, and sebaceous cysts grouped together accounted for 17.3% of the lesions. The percentage incidence of correct diagnoses ranged from 4% for the epidermoid cysts to 70% for the dermoid cysts. Aids in the diagnosis of dermoid cysts were factors of age and location. Sixty per cent of the dermoid cysts occurred in patients in the first decade of life, and 75% of them were on either the brow or the upper lid. Nineteen lesions were xanthelasmas, too few in number to warrant statistical consideration. However, all of these were correctly diagnosed clinically. Fourteen of the 19 lesions involved the upper lid.

The Management of Endophthalmitis Following Cataract Extraction. G. Pico. A. M. A. Arch. Ophth. **59**:381-385 (March) 1958 [Chicago].

In the course of 740 cataract extractions carried out by the author between 1948 and 1956, endophthalmitis developed in 5 patients. The author states that this incidence of 0.65% is in accord with that in most other recently reported series. Only a limited number of cases are on record in which endophthalmitis complicating cataract extraction has been treated successfully. In 2 of the author's 5 patients with intraocular infection, managed, respectively in 1951 and 1952, the end-result was phthisis bulbi. In the light of present knowledge, it is clear that the dosages of penicillin and chloramphenicol employed were not adequate. With the advent of the newer antibiotics, the prognosis seems somewhat improved. Either chloramphenicol or tetracycline is the antibiotic of choice, since both have the ability to penetrate through the blood-aqueous barrier when they are given in massive dosages. Both have broad antibacterial spectrums, and both are effective when administered orally. The use of a corticosteroid with the antibiotic is recommended, as it will produce a rapid diminution of the inflammation and thus prevent the destruction of the retina and choroid.

In 2 of the 3 patients treated respectively in 1954, 1955, and 1956, the outcome was happier. In each instance treatment was instituted immediately after endophthalmitis appeared in the form of a vitreous abscess. Initial improvement was evident within 24 to 48 hours after therapy was begun, and in the course of 2 or 3 weeks the vitreous gradually cleared. The oral dosages of both the antibiotics and the corticosteroids were gradually diminished as the eye quieted down and vitreous clearing became evident. In the remaining patient treatment was along the same lines, but the final vision was limited to finger count, not, it was believed, because of the intraocular infection but because of a retinal detachment, which was probably related to loss of vitreous at operation.

Variability of Accommodation During Steady Fixation at Various Levels of Illuminance. M. Alpern. J. Optic. Soc. Am. **48**:193-197 (March) 1958 [Lancaster, Pa.].

By means of a stigmatoscope imaged by an optometer arrangement, the variability of the dioptric power of the eye during steady fixation was measured for 4 practiced observers over a range of intensities from 2.5 to 3 log photons (trolands) of retinal illuminance in one-half logarithmic steps. Two different viewing conditions (constant-size and variable-size test letters) were studied, but no significant difference between them was obtained. There was almost a 4-fold decrease in the variability of 10 optometer settings as the intensity was increased over this range. There was a sharp transition at 1 photon, suggestive of a discontinuity between scotopic and photopic vision. These changes could be eliminated by cycloplegia of the fixating eye. Essentially the same results were obtained when the refraction of 1 eye was measured objectively with a coincidence optometer, while the other eye fixated the chart. This latter technique is,

however, less valid at the lower intensities because of the tendency to fixate the measuring light of the optometer.

These observations show that the dioptric power of the human eye is changing continuously even during the steadiest of fixations. The fluctuations in accommodation will at a given moment produce a distribution of intensity slightly defocused from the optimum distribution. Whether the eye is defocused positively or negatively, the fluctuations of accommodation will constantly change the distribution of intensity in the retinal image. A theory is developed which accounts for the limits of fluctuation as a special example of intensity discrimination. This theory postulates that the limits of fluctuation are proportional to the critical value of the quotient obtained by dividing the intensity difference threshold by the intensity of retinal illuminance. This theory suggests a possible explanation for the response of the accommodation of the eye to the addition and removal of a minus lens, and thus leads to a hypothetical answer to the theoretical question, "What is the stimulus to accommodation?"

INDUSTRIAL MEDICINE

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What are the health factors to be considered in the placement of personnel? What evidences of health impairment should one seek in periodic medical checkups? So far as the author is concerned, answers to these questions are not available. If there are health hazards in the "executive" environment, then the so-called executive health examination is a legitimate part of occupational medicine. The health status of 2 groups of employees (176 men in each) was examined. The first group was labeled "management" or "executive" purely on the basis of personnel classification data. The second group, labeled "control," was chosen at random from the remaining employees on the basis of age alone. Each man was examined 2 or more times by 1 of 3 board-certified internists who work on a full-time basis in the medical department of an oil company. The extent of individual examinations was left to the discretion of the individual physicians. The following procedures were fairly routine: (1) a detailed history emphasizing the occupational and social factors; (2) a complete physical examination of the disrobed patient, including digital rectal examination; (3) red blood cell count, hemoglobin level, white blood cell count, sedimentation rate, and packed cell volume; (4) urine examination, including microscopic examination of the sediment; (5) stool examination for occult blood; (6) electrocardiogram; and (7) x-ray examination of the chest. Further examinations included gastrointestinal x-ray series and gallbladder series; proctoscopy and sigmoidoscopy, especially on men over 40 years of age or anyone having blood in the stool; ballistocardiography; exercise tolerance test; determinations of protein-bound iodine and blood cholesterol; and cystoscopy. These additional tests were chosen on the basis of the examining physician's findings in the more or less routine part of the examination.

A table that lists the diseases occurring in 10% or more of both groups of men shows that obesity existed in 30.9% of the executives and in 32% of the controls. For arthritis and rheumatism the executive and control percentages were, respectively, 21.2 and 11.2%; for hemorrhoids, 20 and 21.3%; for arteriosclerosis, 19.4 and 19.5%; for hypertensive disease, 19.4 and 18.9%; for anxiety states and neuroses, 19.4 and 13%; for back symptoms, 11.5 and 5.9%; and for hay fever, 10.3 and 11.2%. There was no clear-cut evidence that the working environment of management or executive personnel had any peculiar hazards. The author believes that, in the absence of such demonstrable hazards, it is unwise for the physician to be dogmatic regarding health factors in the selection of executives. Nor is it wise for the physician to narrow his health evaluation to any specific variety of disease process. Rheumatic complaints and disease were significantly more frequent in the executive or managerial group than in the control group. This will be investigated further.

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The author observed 30 patients with carbon monoxide poisoning in the course of the last 3 years. Observations on these and on 11 others observed by members of his medical group are re-

viewed. It is pointed out that the diagnosis of carbon monoxide poisoning can be based on the following criteria: 1. The blood level of carboxyhemoglobin is 10% or more. 2. Symptoms of vague ill-health usually include 1 or more of such complaints as headache, anorexia, dyspepsia, weakness, and dizziness. 3. The symptoms should clear 4 to 7 days after removal from exposure and after daily inhalations of carbogen for 1 hour. (The addition of carbon dioxide to the mixture increases the respiratory rate and facilitates the dissociation of carboxyhemoglobin.) 4. No other medication is necessary. 5. The patient is symptom-free when the blood level of carboxyhemoglobin is reduced to below 10%.

The 41 patients fell into 3 environmental categories: (*a*) garage workers; (*b*) drivers of vehicles (trucks, tractors); and (*c*) housewives. Operators of farm tractors accounted for a large number of cases. Many diesel farm tractors have a vertical exhaust stack no higher than the driver's head. The driver may complain of headache and malaise after a prolonged period on the tractor. In enclosed vehicles the source may be a defective manifold or muffler. Housewives comprised 25% of the cases. Washing machines operated by gasoline engines caused illness in some. In 1 instance the use of a gas-heated iron produced toxic concentrations of carbon monoxide. A frequent offender has been a "space heater" type of oil stove located in the family living room. The toxicology of carbon monoxide is discussed, and it is pointed out that provincial laboratories in Canada are equipped to determine the carboxyhemoglobin content of the blood. Compensation boards will now accept claims for illness arising out of exposure to carbon monoxide on the job.

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Skeletal Alterations in Patients with Decompression Illness. C. Garavaglia. Minerva med. **49**:172-175 (Jan. 17) 1958 (In Italian) [Turin, Italy].

Liberated gas bubbles remain longer in the bone marrow than in other tissues in persons affected with decompression illness. Occlusion of the terminal arterioles of the bones causes aseptic necrosis. The author presents the roentgenologic findings of bone lesions in 2 patients with decompression illness. The first patient was a 30-year-old man who had been working in caissons for 10 years. After the 5th occupational year he has begun to have pain in the joints, accompanied by otorrhagia, vertigo, and paracusis. Roentgenologic findings showed pseudocystic epiphysial alterations in the head of the right humerus and in both heads of the femur. No articular lesions were detected. The other patient was a 52-year-old man who had worked in caissons for 26 years. The first symptoms of decompression illness appeared 6 years after he started work and consisted of acute manifestation of decompression with pain in the right leg and in both knees. Muscle and joint pains have recurred frequently, which induced the patient to leave this occupation. During the last working years the joint disease had intensified and the right leg became shorter, resulting in limping. The roentgen-ray picture showed an almost complete disappearance of the head of the femur. This bone state is similar to an outcome of Perthes' disease. Persistence of pseudocystic areolae in the remnants of the head of the femur is a definite differentiating feature of the presence of decompression illness from Perthes' disease.

Prognosis and Work Capacity After Cardiac Infarction. E. Iisalo, H. Kalliola, A. Kasanen and E. Linko. Nord. med. **59**:264-267 (Feb. 13) 1958 (In Swedish) [Stockholm].

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THERAPEUTICS

Chlorpromazine Jaundice: The Effect of Continued Chlorpromazine Ingestion in the Presence of Chlorpromazine Jaundice. E. M. Schneider, C. Daugherty and J. K. DeVore. South. M. J. **51**:287-291 (March) 1958 [Birmingham, Ala.].

It has been estimated that jaundice occurs in approximately 1% of all patients receiving chlorpromazine. This jaundice has the character of an intrahepatic obstructive lesion. Treatment is largely empirical, but it is generally accepted that, when jaundice appears, the drug must be withdrawn. The present report is based on a study of 4 patients

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Of the patients with cardiac infarction treated in the medical clinic in Åbo from 1952 to 1956, 370 were discharged as convalescent. From 6 months to 5 years later, 242 patients were reexamined, 41 were lost to observation, and 87 had died. Of the 242 patients, 60.7% reported return to regular work, mostly from 3 to 6 months after discharge, and 39.3% were unable to work. Sixty-eight patients were readmitted because of certain or suspected recurrence of cardiac infarction; 31 of these belonged in the poor-risk group. Digitalis treatment after discharge in cases of cardiac insufficiency was often found to be unsatisfactory, pointing to the need of more effective supervision of after-treatment. Two-thirds of the patients whose electrocardiograms revealed persisting auricular fibrillation and two-thirds of those with persisting QS pattern in the unipolar chest leads considered themselves capable of work. Of the 87 patients who died, 60 were in the poor-risk group and 27 in the better group. All the deaths occurred within the first year after the infarction. The mortality increased with age. The patients in the poor-risk group who became able to work have, for the most part, done unexpectedly well, even in physically hard work.

THERAPEUTICS

Chlorpromazine Jaundice: The Effect of Continued Chlorpromazine Ingestion in the Presence of Chlorpromazine Jaundice. E. M. Schneider, C. Daugherty and J. K. DeVore. South. M. J. **51**:287-291 (March) 1958 [Birmingham, Ala.].

It has been estimated that jaundice occurs in approximately 1% of all patients receiving chlorpromazine. This jaundice has the character of an intrahepatic obstructive lesion. Treatment is largely empirical, but it is generally accepted that, when jaundice appears, the drug must be withdrawn. The present report is based on a study of 4 patients

in whom the administration of chlorpromazine was continued without change after the appearance of jaundice. All 4 patients were inmates of a state mental hospital; 3 were women and 1 a man. All 4 patients had been receiving chlorpromazine in dosages of 150 to 200 mg. per day for 25 to 39 days prior to the appearance of jaundice. In each instance, chlorpromazine was continued without change in dosage until all clinical and laboratory evidence of jaundice had disappeared. On 3 of the 4 subjects, laboratory studies and biopsies of liver specimens were obtained within 3 to 5 days of the appearance of jaundice. In patient 2 there was a 12-day interval between the onset of icterus and the initial laboratory study. A liver biopsy attempt on this patient was unsuccessful. A second series of liver function tests was obtained on all patients 10 to 21 days after the initial observations. A third battery of hepatic function tests, together with liver biopsies on all subjects except patient 2, was performed 42 to 68 days later and was the final study on subjects 2, 3, and 4. Patient 1 was subjected to 1 additional series of liver function tests 151 days after the onset of jaundice.

Elevations of serum alkaline phosphatase and serum bilirubin levels were noted in all subjects initially. The bilirubin levels tended to return to normal somewhat earlier than did the alkaline phosphatase levels. In all patients serum lipid phosphorus determinations were higher during jaundice than after recovery. Liver biopsies were available on 3 of the 4 subjects during and again after clearing of jaundice. Bile canalicular plugging and periportal infiltration were noted in 2 subjects on the first biopsy but were normal on repeat examination. The third subject showed only some fatty change in both biopsies. In the present group of patients chlorpromazine therapy was continued with impunity after the appearance of chlorpromazine jaundice. The possibility of chlorpromazine inducing changes in bile viscosity or composition and in biliary sphincter tone was neither supported nor refuted by this study. However, the available data do cast doubt on the likelihood of chlorpromazine jaundice being due to hepatotoxicity or chlorpromazine sensitivity or to existing hepatic disease.

Cytostatic Medicaments and Malignant Tumors: Clinical Results of Trials Carried On for Four Years. A. Ravina and M. Pestel. Presse méd. **66**:313-314 (Feb. 22) 1958 (In French) [Paris].

The records of 120 patients treated with cytostatic preparations for various types of cancer show that the actinomycins C and D are, on the whole, the easiest to manage. Hemorrhagic complications have been reported but are generally believed to occur less often than with most other cytostatics, especially nitrogen mustard. The other manifestations of intolerance, which consist chiefly of irritation of the digestive mucosa with stomatitis, anorexia, nausea, abdominal pain and diarrhea, and more or less extensive alopecia, are always transitory and comparatively easy to control or avoid. The best results were obtained in patients with lymphatic disorders, such as chronic leukemia or Hodgkin's disease, but in certain patients with other malignant conditions the actinomycins also proved beneficial, checking the malignant process and assuring survivals that were sometimes prolonged.

R 261 (N-desacetylthio-colchicine), a synthetic sulfurated derivative of colchicine, with greater antimitotic power and less toxicity than colchicine, was given intravenously to 20 patients. Several failed to show any improvement; in 2 who had bronchial cancers the tumor seemed to regress, but the treatment had to be discontinued because of the intense leukopenia to which it gave rise; and in a few others the progress of the disease was checked for periods of varying length. R 261 in a 2.5% pomade may also be applied topically to superficial or cutaneous cancers, either primary or metastatic, whether or not they are ulcerated. The potency of the drug, however, makes it hard to manage and in 2 of the authors' patients it led to shallow but extensive ulcerations that pursued a torpid course. An interesting point that should be further investigated is the fact that R 261 is capable of causing paroxysmal pain in the tumor and also in its metastases, the existence of which was sometimes revealed by this means. Similar focal pains have been noted, but very rarely, after the administration of actinomycin or E 39 (5-amino-7-hydroxy-imine 2,5-depropyloxy-3-6-benzoquinone), another cytostatic now being studied by the authors.

Azan (8-azaguanidine, sodium 5-amino-7-hydroxy-triazolopyrimidine) may inhibit the growth of certain cancer cells by acting on the purine metabolism. Well-defined regression of the functional and general symptoms, obtained by its use in a few patients, was never accompanied by any appreciable change in the size of the tumor. The number of patients who were given azan for malignant lymphatic conditions, for which the drug is chiefly indicated, was, however, very small.

Exophthalmos of Graves' Disease: A Summary of the Present Status of Therapy. E. P. McCullagh, M. Clamen, W. J. Gardner and others. Ann. Int. Med. **48**:445-470 (March) 1958 [Lancaster, Pa.].

The authors report on 39 patients with exophthalmos of toxic diffuse goiter (Graves's disease), 20 of whom were treated with L-triiodothyronine, 10 were treated with both corticotropin (ACTH) and hydrocortisone, and 9 were subjected to pituitary surgery in an attempt to reduce extremely

severe exophthalmos. Of the 20 patients with progressive exophthalmos treated with L-triiodothyronine for periods ranging from 2 to 11 months, the proptosis was reduced by 2 mm. or more in 9 patients, remained stationary in 9, and became worse in 2. The aim was to give L-triiodothyronine in the largest dose that the patient could tolerate with comfort, usually 100 mcg. per day (range, 75 to 200 mcg. per day). Six of the 9 patients showing significant recession did so at their first visit, 2 months after treatment was started. Each of the 10 patients treated with both ACTH and hydrocortisone received 50 mg. of ACTH intravenously for a period of 6 hours daily for from 5 to 16 days, and 200 mg. of hydrocortisone orally daily; the dose of the latter drug was reduced over a period of weeks. Duration of follow-up ranged from 1 to 4 months. There was symptomatic improvement in all 10 patients. The sense of conjunctival irritation, lacrimation, and any ocular pain that had been present usually diminished greatly or disappeared in from 1 to 3 days after treatment was instituted. Conjunctival and lid swelling apparently diminished in all but 1 patient. There was dramatic improvement in the proptosis as well as in the soft tissue swelling in only 2 of the 10 patients; active hyperthyroidism was present in these 2 patients.

Of the 9 patients subjected to pituitary surgery, 5 were operated on before 1946 and 4 were operated on since 1953 when adequate replacement therapy for severe pituitary failure had become available. The surgical procedures in these 9 patients included some combination of section of the pituitary stalk, cauterization of the anterior lobe, and placement of an impervious diaphragm of plastic, waxed paper, or tantalum above the sella turcica in the hope of interfering with regeneration of the "portal circulation" of the pituitary. In all 9 patients the exophthalmos improved postoperatively; in some it disappeared entirely, and visual acuity that had been extremely poor returned to normal.

The measures employed in the treatment of exophthalmos of toxic diffuse goiter should be chosen with care, chiefly on the basis of the severity or type of ocular changes and the rate and degree of progression of the disease. Estrogens and androgens as pituitary inhibitors have been of little or no value in the treatment of exophthalmos. Roentgen-ray irradiation of the pituitary gland may also be considered to be of little value, since heavy doses of this therapy do not produce hypopituitarism. If exophthalmos is the first evidence of toxic diffuse goiter and hypometabolism exists with it, the administration of desiccated thyroid, of thyroxin, or L-triiodothyronine, in at least a physiological dose, is indicated. If exophthalmos is increasing in severity, it is advisable to give thyroid hormone in larger than physiological doses up to the amount that can be tolerated by the patient without undesirable side-effects. In patients having severe swelling of the lids and conjunctivas, the use of ACTH and cortisone may be valuable. It is considered important to limit the intake of sodium to 500 mg. per day and to add several grams of potassium to the daily intake while ACTH and cortisone are being used; the use of an ulcer regimen also is advisable, if large doses of these hormone preparations are used. In severe cases of exophthalmos not responding to other measures of treatment, pituitary surgery may be considered. Experience with this type of treatment to date is small but encouraging. In the event of extremely rapid progression of the disease, when loss of 1 or both eyes is seriously threatened, orbital decompression may become imperative.

Value of Aminopyrine. L. Cardon, O. H. Comess, T. A. Noble and M. M. Pomarane. Ann. Int. Med. 48:616-634 (March) 1958 [Lancaster, Pa.].

The authors report on 3 men and 3 women, between the ages of 33 and 51 years, with various febrile diseases to illustrate the potent antipyretic effect of aminopyrine. Of the first 3 patients, 2 had prolonged intractable fever of unknown origin but most likely due to acute exacerbation of rheumatic fever, and 1 had periarteritis nodosa with spiking fever. Aminopyrine, in doses of 5 grains (0.32 Gm.) 3 times daily and 10 grains (0.65 Gm.) 4 times daily, was the only drug which controlled the fever and reversed the progressive downhill course of the disease after weeks of ineffective therapy with large doses of chemotherapeutic and antibiotic agents. In these 3 patients the action of aminopyrine simulated that of a specific drug and proved to be lifesaving. Granulocytopenia did not occur in these patients, although the drug was given continually for up to 5 months to 2 patients and intermittently for up to 2 years to 1 patient. A tendency to leukopenia in 1 patient was readily controlled by reduction in dosage. The 4th patient with ulcerative colitis, rheumatic heart disease, and mitral stenosis received 5 grains (0.32 Gm.) of aminopyrine 4 times daily, affording a dramatic respite from fever which was refractory to all other treatment, including antibiotics and corticotropin (ACTH) for 17 days. During this respite the patient recovered much weight and strength and was thereby in much better condition to withstand the operation for perforation of the colon which occurred later on. Persistent spiking fever subsided by lysis as a result of treatment with 5 grains (0.32 Gm.) of aminopyrine 4 times daily in the 5th patient with carcinoma of the head of the pancreas. The 6th patient also had carcinoma of the head of the pancreas, with metastasis to the liver, associated with persistent spiking fever which had been re-

fractory to prolonged treatment with penicillin, chloremphenicol, oxytetracycline (Terramycin), and aspirin. The temperature was restored to normal by treatment with aminopyrine.

Aminopyrine is of value particularly in conditions not amenable to therapy with specific chemotherapeutic and antibiotic agents or in patients in whom these prove to be ineffective, in patients in whom other antipyretics are not tolerated or in whom they have failed, or in patients in whom it is not advisable to assume the risks of therapy with corticotropin and the corticosteroids or in whom these agents have failed. Aminopyrine is still a uniquely valuable and occasionally a lifesaving antipyretic which deserves a trial whenever fever is a significant feature of the clinical picture of the disease. The danger of granulocytopenia from the use of aminopyrine, although real, has been overemphasized and is no greater than from many other drugs in common use today. Aminopyrine has its place in therapeutics under well-controlled clinical conditions and under supervision of a physician, but its careless and indiscriminate use is to be condemned.

PATHOLOGY

Cryptic Cervical Nodal Metastases: A Pathologic Study of Possible Primary Sources. M. S. Comess, M. B. Dockerty, and O. H. Beahrs. Arizona Med. **15**:87-95 (Feb.) 1958 [Phoenix].

The authors studied 1,189 patients with proved metastases to cervical lymph nodes, who were seen at the Mayo Clinic between 1945 and 1953. In 103 (8.7%) of these patients, the primary source of carcinoma spreading to cervical lymph nodes could not be found at the initial investigation. Three patients could not be traced. The remaining 100 patients were subdivided into 3 groups: 1. A primary tumor was discovered at some time subsequent to the original examination in 40 patients. 2. Forty-four patients died without evidence of the source of the metastasis. 3. Sixteen patients were living and had no further evidence of malignant disease. If careful history, minute physical examination, and appropriate endoscopic, roentgenologic, and hematological studies are unavailing, the source for the presumed metastasis may be considered occult. Surgical exposure and histological diagnosis are considered essential in the management of a cervical tumor, the nature of which is indeterminate after clinical study. Fresh frozen sections are of decided help when, as is frequently the case, a definitive diagnosis can be made immediately by this method. Indicated operative procedures may be immediately performed. The histopathological findings were often of help in locating a cryptic primary tumor, particularly 1 in the thyroid gland. The histological type and grade of the secondary lesion determine in large part the prognosis and management of the individual case. Metastases of high-grade squamous-cell carcinoma in the submaxillary and upper deep jugular chains were found to imply unexpectedly favorable prognosis. Long-term survival without further evidence of neoplastic disease after varying treatment was noted in about 33% of patients with such lesions. No adequate explanation of the source of these tumors is available.

A Statistical and Histological Survey of Metastatic Carcinoma in the Skeleton. P. C. Meyer. Brit. J. Cancer **11**:509-518 (Dec.) 1957 [London].

The histological files of a London hospital, which contained records of 14,154 autopsies from 1946 to 1955, inclusive, revealed 320 cases with skeletal involvement by secondary carcinoma. During the same period surgical material was obtained from only 20 cases of metastatic carcinoma in bone; the latter are not included in the present study. Although the skeleton is not examined routinely in all cases, a standard technique is employed. An examination of the relevant parts of the skeleton is carried out if justified on clinical or radiologic grounds or if there is evidence of any bone lesion at autopsy. Care was taken to exclude examples of direct skeletal involvement by carcinoma. The site and nature, whether of compact lamellar or cancellous type, of each portion of bone examined histologically were noted, and a quantitative estimate of the degrees of resorption and new bone formation was carried out. It was found that changes involving different bones in the same patient were remarkably consistent. The 320 cases are tabulated according to the location of the primary tumor. The findings in 2 comparable series of cases investigated by other authors are shown in the same table. The primary tumor was found in the bronchus in 124 of the patients, in the breast in 56, in the prostate in 53, in the stomach in 33, in the intestine in 11, in the kidney in 10, in the liver and bile passages in 6, in the thyroid in 4, and in smaller numbers in pancreas, esophagus, and uterus.

The author regards the 33 cases secondary to gastric carcinoma as surprising, since ordinarily gastric carcinoma is not generally considered as a frequent source of skeletal metastases. The low figures for renal and thyroid carcinomas are of great interest and reflect the low incidence of these conditions in the general population. Osteoclastic erosion was the main factor in resorption of bone, but a direct osteolytic action was frequently exerted by the stromal cells of the tumor. In many instances resorption of bone appeared to be the result of di-

rect pressure by masses of proliferating epithelial cells. Osteosclerosis was produced by the apposition of new bone on existing trabeculae and by the formation of new trabeculae as a result of metaplasia of marrow cells. A complete absence of bony reaction or only a slight reaction was frequently observed in patients with the oat-cell variety of bronchial carcinoma, while a relationship between osteosclerosis and a high degree of histological differentiation could be established in the case of mammary and prostatic carcinoma.

Muscle Involvement in Boeck's Sarcoid. S. L. Wallace, R. Lattes, J. P. Malia and C. Ragan. Ann. Int. Med. **48**:497-511 (March) 1958 [Lancaster, Pa.].

Between 1946 and 1956, random muscle biopsies were done for diagnostic reasons on 42 patients with sarcoidosis at the Presbyterian Hospital of New York. The patients in this group showed a clinical picture compatible with sarcoidosis; 32 of them had, in addition, pathological proof of the diagnosis, and the remaining 10 had a positive reaction to the Kveim test in the absence of pathological evidence of the disease. None of the biopsy specimens were taken from an area with objective clinical abnormality. They were taken most commonly from the gastrocnemius muscle because of its greater accessibility, although biopsy specimens also were obtained from the deltoid, pectoralis major, sternocleidomastoid, and platysma muscles and from otherwise unidentified muscles of the neck.

Twenty-three of the 42 patients with sarcoidosis showed pathological changes compatible with this diagnosis on biopsy of tissue from skeletal muscle. Four patients had sensations of muscle pain or aching, and 2 of these had sarcoid granulomatous lesions on biopsy. Six patients had migratory polyarthritis, and 5 of them had muscle biopsies showing sarcoid granulomatous lesions. Seventeen patients with sarcoid lesions in the muscle had no muscle or joint symptoms whatever. There was no consistent correlation between objective changes in the muscle and the presence of lesions. Six of 17 patients with 1 or 2 organs involved by sarcoidosis had a positive muscle biopsy; 17 of 25 patients with 3 or more organs or systems involved by sarcoidosis showed sarcoid granulomatous lesions on muscle biopsy. The wider the dissemination of the sarcoidosis, the more likely the muscle biopsy was to show sarcoid lesions. The sarcoid granuloma in muscle was similar to that in other tissues. One patient had a granulomatous arteritis in the muscle due to sarcoid. There was no relation between age, sex, or race of the patient and the presence or absence of sarcoid granulomatous lesions on biopsy. Because of sparsity of lesions, routine sectioning at multiple levels proved to be of great importance in discovering sarcoid lesions in muscle. Although sarcoid granuloma is not specific for sarcoidosis, the use of muscle biopsy is indicated as an aid in diagnosis of sarcoidosis, particularly if no other histological specimens are available for examination.

RADIOLOGY

Treatment of Carcinoma of the Breast with Roentgen Therapy Alone. V. Racugno and A. Angei. Rass. med. sarda **59**:497-506 (Sept.-Oct.) 1957 (In Italian) [Cagliari, Italy].

Baclesse, in France, and Nuvoli, in Italy, contend that roentgenotherapy can substitute for surgical treatment in both operable and inoperable types of carcinoma of the breast. This opinion led the authors to use roentgenotherapy in 17 patients during the period between 1953 and 1956. Seven patients had inoperable neoplastic lesions, some with ulcerations and extensive regional metastases. The other patients had the operable type of tumor. Biopsy by aspiration was performed in 14 patients with nonulcerative type of carcinoma. Histological findings revealed the presence of adenocarcinoma. The radiation was delivered from a 180-kv. x-ray machine. The filtration was 0.25 mm. Cu plus 1.0 mm. Al; the focus-skin distance was 40-50 cm. The treatment was carried out in 4 areas; the breast was irradiated through 2 opposite sections, 1 medial and 1 lateral, at a total rate of about 5,000 r.

Of 7 patients with inoperable tumors, 4 died within a period of 8 months to 2 years after discontinuance of the roentgenotherapy. The primary neoplastic lesion and regional metastases disappeared in 2 patients, but they died from pleuropulmonary involvement of the opposite side. All 10 patients with tumors classed as operable are still alive with no recurrence or metastasis in a period of 1 to 3 years after discontinuance of roentgenotherapy. The primary tumor and regional metastases have disappeared completely only in a few patients; in the others the lesions have been considerably reduced in size. The systemic reaction to the therapy in all patients was mild; local reaction was marked, but it subsided after the termination of treatment. Small residual areas of epitheliosis were observed in 3 patients, but these disappeared after topical medication for a few months.

Roentgenotherapy for Fibromyoma of the Uterus. B. Vidal and G. Englaro. Minerva med. **49**:98-104 (Jan. 13) 1958 (In Italian) [Turin, Italy].

Roentgenotherapy was given to 239 patients with fibromyoma of the uterus at the General Hospital at Udine during the last 25 years. One hundred

forty-three women (62%) were in their 40's, and 53 women (23%) were in their 50's. Small-sized fibromyomas were present in 76 patients (33%), medium-sized ones in 105 (45%), large-sized ones in 44 (19%), and very large fibromyomas in 7 (3%). Large-sized tumors were prevalent in women over 60 years old and medium-sized tumors in all other age groups. Sixteen patients did not complain of hemorrhage. Surgical therapy was contraindicated in about one-fourth of the patients. Regression in the size of the tumor occurred mostly in a period between the 3rd and the 6th month of therapy. No recurrence of tumor was observed, which was partly due to the castration caused by the roentgenologic procedure. The radiation was delivered from a 180-kv. x-ray machine. The filtration was 0.5 mm. Cu plus 0.5 mm. Al; the focus-skin distance was 40 cm. Total surface dose varied between 1,000 and 1,200 r per area when 4 portals were employed and between 1,500 and 1,800 r per area when 2 portals were employed.

Almost complete regression of fibromyoma and complete subsidence of hemorrhage and of associated symptoms were observed in 122 patients (53%), partial regression of fibromyoma and complete subsidence of hemorrhage in 110 patients (47%), and insignificant or no regression of fibromyoma and complete subsidence of hemorrhage in 7 patients (3%). Contact was lost with 7 patients after termination of the treatment. The best results were obained in those instances in which roentgenotherapy has suppressed ovulation. Good results were also obtained in 28 women in menopause; among these there was almost total regression of tumor in 10, partial regression in 13, and insignificant or no regression in 5.

PUBLIC HEALTH

Fluoridation of Public Water Supplies and Its Relation to Musculoskeletal Diseases. C. L. Steinberg, D. E. Gardner, F. A. Smith and H. C. Hodge. New England J. Med. **258**:322-325 (Feb. 13) 1958 [Boston].

The authors estimated the fluoride content of ash in 18 various bone samples obtained at autopsy or through surgical intervention from 14 patients, 13 of whom had various forms of arthritis, 1 of whom did not have arthritis, but all of whom had ingested fluoridated water for a period ranging from 3 years and 5 months to 4 years and 7 months. No excessively high concentration of fluoride was found in any of these specimens. Fifteen various bone samples obtained from 11 patients with various forms of arthritis and from 2 patients who did not have arthritis, all of whom were residents of a nonfluoridated water area, were analyzed for fluoride content expressed in parts per million of ash. The fluoride concentration value in bone of the residents of the area in which the water was not fluoridated and that of the residents in the fluoridated water areas were not statistically different. A careful review of the roentgenograms of both these groups, along with the bone fluoride content studies, failed to reveal any relation between various forms of arthritis and the ingestion of fluoridated water as recommended by health authorities.

The Risk of Ascaris Infestation From the Use of Human Sludge as Lawn Fertilizer. J. O. Bond. J. Florida M. A. **44**:964-967 (March) 1958 [Jacksonville].

The modern sewage treatment process does not necessarily completely destroy all pathogenic organisms. An example is the municipal sewage disposal plant in Tampa which sells sludge to a local nurseryman who, in turn, retails it as lawn fertilizer. During the summer this arrangement was initiated, a local pediatrician treated a child with severe ascariasis and, in a careful history, obtained the information that the child had had contact with a lawn fertilizer obtained from this source. This paper is a report on the subsequent investigation to determine whether this sewage sludge was a source of infection due to Ascaris organisms in this community. Specimens of sludge were obtained at approximately biweekly intervals from the Tampa Municipal Sewage Disposal Plant, where sludge is removed from the settling basins, allowed to digest at 26.6 to 32.2 C (80 to 90 F) for approximately 30 days, and distributed to beds for drying up to 21 days. After determination of moisture content, the specimens were examined for Ascaris ova by the standard zinc flotation method and by quantitative Stoll counts. Three specimens each were taken from the raw, the digested, and the drying sludge. Dried sludge was the only source of plain commercial sludge for lawn fertilizer. Viable Ascaris ova in the range of 100 per milliliter were shown to be present in sewage sludge sold as lawn fertilizer in Tampa.

The second part of the investigation was to determine whether the children exposed to sewage sludge used as lawn fertilizer were actually infected by the ova known to be present. Two groups of children, who were alike in all respects except exposure to the fertilizer, were studied for prevalence of infection due to Ascaris organisms. No significant difference was found in the prevalence of the infection in these two groups of children, so that the sewage sludge used as lawn fertilizer was a potential, but not an actual, source of ascariasis in this community. Heat sterilization of the sludge for a minimum of 3 minutes at 65 C (149 F) would eliminate this potential hazard.

BOOK REVIEWS

Foundations of Neuropsychiatry. By Stanley Cobb, A.B., M.D., Sc.D. Sixth edition of work formerly known as A Preface to Nervous Disease. Cloth. $5. Pp. 313, with 16 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1958.

This authoritative book is small and easy to read. It contains an immense number of facts organized into a clear pattern, and the whole work is illuminated by the understanding that the author brings to his subject. The artificial barriers between neuropathology, neurophysiology, neurology, and psychiatry do not trouble him; he hurdles them easily and manages to achieve a satisfying synthesis of the classical anatomic point of view and the most modern functional concepts. The nonexpert should find this book useful either as an introduction or as a review. It touches on almost everything that has been thought and said about the central nervous system—makes it live and gives it meaning. The expert will be fascinated by the author's insight, his reasonableness, the skill with which he writes, and his mastery of his material. In a few places the expert may disagree with the author, but he will be interested to find the cause for the disagreement. The author is such a knowledgeable person that if the truth escapes him it is indeed elusive.

Chapters 1 through 5 show how the nervous system is built of simpler structures and how complex functions are organized. These chapters include much factual material on the autonomic nervous system, the localization of function in the brain, and relevant neuroanatomy. The author is at his best in chapter 6, where he argues in favor of abandoning the dichotomy, organic versus functional, which encumbers our thinking and seriously impairs an understanding of the brain. He propounds the advantages of a holistic approach in a way that is both interesting and convincing. The broad and inclusive frame of reference he recommends permits a complete statement of what the brain is and does. A narrower frame of reference would leave out much that is essential and show only a partial and distorted picture. Subsequent chapters deal with cerebral circulation, cerebrospinal fluid, disease states, psychological concepts, and psychopathological reactions. Neurochemistry is touched on rather lightly. This is unfortunate, because the basic unity of structure and function which the author sees so clearly is most evident when the brain is viewed on a molecular or submolecular level. At this level, structure and function are one and the holism for which the author argues is not a philosophical concept but a fact. If this book does not deal as extensively with brain chemistry as some might wish, it goes about as deep as is practicable for anyone who wishes to keep his feet on the ground of present-day neurology and view the peaks of psychological psychiatry. In the next edition, there will doubtless be longer sections on brain chemistry, for this is an area of knowledge that is growing rapidly. The brain can be compared to a telephone exchange, a calculating machine, a constellation of psychological constructs; but it is primarily a chemical organ.

Adventures in Medical Education: A Personal Narrative of the Great Advance in American Medicine. By G. Canby Robinson, M.D., LL.D., Sc.D. Cloth. $5. Pp. 338, with illustrations. Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass., 1957.

This is the autobiography of a man whose career interests were in academic medicine at the time in which medical education was rapidly changing. The author began his medical study at the Johns Hopkins Medical School in 1899 as one of the 50 students in that institution's seventh class. This new medical school and its talented faculty, which were destined to exert a major influence on medical education in the United States, is pictured as seen by students in its early and formative days. The author believes that "the medical school had the social and intellectual spirit of a true university graduate school. Students were treated as mature men and women, and the teaching staff helped them to get the best medical education that each was capable of acquiring largely through his own efforts." His description of the course of study and the relationships of faculty and students represents an educational program and environment that, by contrast, clearly places the educational activities of many medical schools today at the undergraduate rather than at the graduate level. After some initial disappointments, described with refreshing candor,

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

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the author went to the Pennsylvania Hospital in Philadelphia for further training. Everyone familiar with this hospital, the oldest in the country, will enjoy learning again of its many fine traditions and possessions. Through subsequent academic and administrative responsibilities at the Rockefeller Institute and at the medical schools of Washington, Vanderbilt, and Cornell universities and Peiping Union Medical College, the author played an active role in many significant developments in medical education. The presentation of these events is enlivened through the recounting of local history, anecdotes, and personal impressions of the many persons who shared these experiences with the author.

Tracheotomy: A Clinical and Experimental Study. By Thomas G. Nelson, Major, M.C., U.S.A.R. Reprinted from American Surgeon, vol. 23, numbers 7, 8, and 9, July, August, and September 1957. Cloth. $3.75. Pp. 111, with 47 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1958.

The available literature dealing with tracheotomy is tremendous. The author had the courage and the energy to tackle this much-discussed subject and present a detailed and comprehensive study. This book starts with the story and evolution of tracheotomy, going from the first authentic discussion by Galen to its presently accepted position. The second part gives a detailed clinical analysis of indications, technique, and complications in 300 patients on whom this operation was performed. Special emphasis is placed on the increase in number and scope of indications not only for mechanical but for a large variety of secretional obstructions. Avoidable technical errors, faulty aftercare, pneumothorax, mediastinal emphysema, and damage to the trachea by ill-fitting cannula are discussed, but little is said about the incidence and nature of postoperative infections of the tracheobronchial tree or, in this otherwise thorough study, the special problems encountered in handling tracheotomies in small children and newborn infants. The final section presents interesting clinical and experimental investigations on dogs, comparing different technical aspects of tracheotomy. The author has laid down acceptable principles of tracheotomy, advocating a transverse skin incision, division of the thyroid isthmus, and excision of a portion of the anterior tracheal wall. While there is nothing startlingly new in this study, this well written work offers a comprehensive and detailed summary of the subject. The book can be recommended not only to the specialist but to anyone dealing with tracheotomy.

Spinal Anesthesia. By John B. Dillon, B.S., M.S., M.D., Professor of Surgery and Chief of Division of Anesthesia, Department of Surgery, University of California Medical Center, Los Angeles. Publication number 326, American Lecture Series, monograph in American Lectures in Anesthesiology. Edited by John Adriani, M.D., Director, Department of Anesthesia, Charity Hospital, New Orleans. Cloth. $3. Pp. 61, with 9 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This monograph was written for physicians who are not board-qualified. It is designed primarily for residents and for the physician who occasionally uses spinal anesthesia. It is carefully written and edited, with a bibliography containing most of the important and classic articles relative to each phase of the problem. Some of the subjects considered include indications for spinal anesthesia; advantages and disadvantages of spinal anesthesia; contraindications to spinal anesthesia; equipment, drugs, and sterilization; general care of patients under spinal anesthesia; and complications of spinal anesthesia. The printing and illustrations are commendable. This book carries out the purpose for which it was designed—that of presenting to the reader in a concise and simple manner the story of spinal anesthesia. Primarily, the salient factors with the important references are presented. It can be recommended for inclusion in medical libraries, for hospitals, and for residents in surgery and in anesthesiology.

Survey of Public Relations Practice in 223 Hospitals. Cloth, loose-leaf. $15. Pp. 119, with illustrations. Trade Cor, Inc., 30 N. La Salle St., Chicago 2, 1958.

This loose-leaf booklet should be read by every hospital administrator. A true picture of public relations is revealed in this comprehensive survey of 223 representative hospitals. According to the report, the most pressing problem in hospital public relations is explaining costs to patients and the public. Other important issues discussed are relationships between personnel and patient and doctors and patient. Methods for fund and money raising are reviewed competently. Tips for improving bulletin boards, Christmas parties, hospital publications, and employee education and morale are intelligently presented. Many excellent ideas for programming, along with specific examples, are included to supplement the survey. These practical ideas are applicable not only to hospitals but to other medical groups as well. Since this book is easy to read, up to date, and well organized, it should be of great value to those interested in developing better public relations.

QUESTIONS AND ANSWERS

USE OF BIOLOGICALS BEYOND EXPIRATION DATE

To the Editor:—*Would gamma globulin with an expiration date of May, 1957, be useless, or would it be of value if the dose is increased by 50 or 100%?*

Mary B. Spahr, M.D., Ithaca, N. Y.

Answer.—The expiration date means the date beyond which the product cannot be expected beyond reasonable doubt to yield its specific results. It is obvious that some products are more stable than others, thus permitting a longer dating period. It is also true that the potency of a product declines gradually with time and does not rapidly diminish at the expiration of the dating period. Additional factors, apart from inherent stability, which are taken into consideration in deciding on the dating period of a product are the type of container, the closure, and the temperature and conditions of storage. The residual potency at any particular time after the expiration date cannot be predicted and could only be determined by the application of specific tests. The expiration date, furthermore, represents the date beyond which the manufacturer does not recommend use of the particular product. In the circumstances, therefore, any use of such a product beyond the expiration date shown on the package would in effect be the sole responsibility of the user.

MANAGEMENT OF THE NEWBORN BABY OF A DIABETIC MOTHER

To the Editor:—*What is the recommended therapy for newborn infants of diabetic mothers?*

Albert C. Merkin, M.D., Las Vegas, Nev.

Answer.—Reis and others (Diabetes and Pregnancy, Springfield, Ill., Charles C Thomas, Publisher, 1952) emphasize that the four real dangers to the newborn infant of a diabetic mother are hypoglycemia, anoxia, lethargy, and prematurity. The characteristic of the newborn infant of the diabetic mother is a marked fall in blood sugar level that occurs within the first hour after birth. This rapidly developing hypoglycemia is not attended by any clinical evidence of the dangerously low blood sugar level except for an early and continuing suckling reflex. Serial blood sugar levels must be determined every 15 minutes during the first hour of life in order to demonstrate this marked fall. This is in sharp contrast to the fall in blood sugar level in the normal newborn infant, which also falls rapidly but not to nearly as low a level as that observed in the newborn infants of diabetic mothers. The hypoglycemia shown to be present during the first hour of life should be prevented by prompt feeding at this time. This may be done by the administration of a few drops of a 50% glucose solution every 30 minutes during the first two hours. The glucose solution may be administered readily by a medicine dropper. The increased suckling reflex aids in this administration. After the first two hours, breast milk, 0.5 to 1 oz., should be alternated with a similar amount of 5% glucose solution every two hours during the first day of life. These may be given by dropper or by bottle, whichever is more convenient. Regular feedings are given every three to four hours beginning on the second day.

Meticulous care must be accorded the clearance of the upper respiratory tract immediately after birth. This can best be accomplished by postural drainage and adequate pharyngeal and tracheal suction. Liberal and prompt use of the tracheal catheter will clear the air passage and improve fetal salvage, but it must be used immediately after birth, whether delivery is vaginal or by cesarean section. The use of the tracheal catheter for clearance of the air passage should always be followed by the administration of oxygen. The apparently oversize and overweight baby of the diabetic mother is often somnolent and lethargic. Its respirations tend to become infrequent and shallow, and its cry is not always as lusty as it might be. This obviously interferes with proper oxygenation. It can be corrected by repeated and continuing external stimulation which will make the infant cry repeatedly and, thus, breathe more efficiently. It may be necessary to continue such repeated external stimulation throughout the first 12 to 24 hours of life. Successful management of the newborn baby of the diabetic mother demands that it be cared for as if it were a premature baby, irrespective of its actual age. This must be done in spite of the usual oversize and overweight. Prematurity is too often overlooked because of the baby's excessive size and weight. Prompt and efficient maintenance of body heat is essential to well-being. This can be accomplished best by immediate transfer to an adequately equipped incubator which will furnish heat and oxygen.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

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CASTRATION AND MENTAL RETARDATION

To the Editor:—*Recently a sex problem has been encountered in a mentally retarded, 37-year-old man. At the age of 10 years this individual was examined at the Stanford-Lane Clinic and was given an IQ rating of 5½ years. He attended a rural school for eight years but made little progress and is at present unable to read and write. From external observation, he appears to be a normal, healthy, adult male, well built, well mannered, and well behaved. A casual observer would suspect nothing abnormal unless he tried to engage the man in conversation. Recently the parents have become quite concerned because of the advances being made by their son toward small female children of neighbors and relatives who occasionally visit. They realize the legal and psychological possibilities involved. They also realize that sterilization by vas ligation or medication is no answer. The extreme alternative of castration is being considered, since institutionalization of this individual would not be warranted. Please give advice on any other way to handle this problem.* *M.D., California.*

Answer.—The first question that comes to mind in such a situation is, "What is the clinical nature of the mental deficiency?" The result of the psychological examination at the age of 10 years really does not constitute a clinical diagnosis. As a first step in the formulation of a plan of action, a restudy of the patient by a physician experienced in the evaluation of mental retardation in adults is indicated. If the patient is as mentally retarded as the test in his childhood seems to indicate, it is quite possible that some of his sexual interests derive from simple sexual curiosity. A physician who has a good relationship with such a patient and who has some aptitude in conversing with mentally retarded individuals could provide him with sexual information and request him to return to talk about sexual matters and sex differences when he wishes. The neighborhood children do need protection, but some of this is the responsibility of the parents of the children and should not be expected to be entirely that of the retarded individual, although, curiously enough, it is this latter viewpoint that prevails in most communities. On occasion, such a handicapped individual is goaded or teased into sexual activity by hostile persons in his immediate environment. The sexual drive of a severely retarded individual is usually not great, so that it again becomes important to evaluate the nature and extent of the retardation at the patient's present age. Decision about castration should be influenced by the extent of the patient's sexual energies and drives and also by the cause of the retardation; for example, familial and, therefore, genetically transmitted mental deficiency would cause more consideration to be given to castration than would the presence of mental deficiency that derives from brain damage.

Answer.—Castration may well constitute mayhem, as defined in the penal code of the state. Regan, in his book, "Doctor and Patient and The Law" (St. Louis, C. V. Mosby Company, 1949), states that the California Penal Code, Section 203, defines mayhem as follows: "One who unlawfully and maliciously deprives another of a member of his body, or disfigures or disables it or renders it useless, etc., is guilty of mayhem."

CLEANING OF OPERATING ROOMS

To the Editor:—*Is it advisable to scrub the operating room floor between each surgical case, or is it sufficient to scrub the floor once a day and in between "dirty cases" only? A question has been raised as to whether mopping introduces more germs between operations than leaving the floors as they are. What is the policy in large teaching hospitals?*

R. P. Froeschle, M.D., Hazen, N. D.

Answer.—The floor is the principal reservoir for dust and bacteria that contaminate operating room air. The operating room floor must be cleaned and disinfected daily. All furniture must be removed to make the entire surface accessible. Trash is picked up with a vacuum cleaner. Shelving, mouldings, and lamps are wiped with a cloth dampened in a quaternary or phenolic germicide. A fresh solution of detergent germicide (quaternary, iodophorm, or phenolic) is made in a clean, 12-qt. pail. One quart of this is spilled in the central work area of the floor. A freshly laundered mophead is used to scrub this area to solubilize dried blood or pus. The remainder of the detergent germicide is then spilled and spread to cover the periphery. After the entire floor is flooded, the film of water is removed with a wet pick-up vacuum cleaner. With minimal study, a pattern can be developed for flooding, spreading, and picking up that avoids walking in the wet area. In large operating room suites, a scrubbing machine that automatically dispenses the detergent germicide is time-saving and convenient. A wet pick-up vacuum cleaner is essential to remove the slurry of dirt and bacteria that is loosened from the floor. In this way, a grossly clean and bacteriologically safe floor is attained. The bacteriological count on the unused surface of the floor 12 hours after this cleaning process should be less than five organisms per square centimeter. There should be no dust. The operating room furniture, including the castors, is wiped with a cloth dampened in a germicide, prior to returning it to the clean room. The center of the operating room floor is cleansed with a mop moistened with detergent germicide immediately

after each operation. This mop is kept in a flushing rim service sink located in the sterilizing room adjacent to the operating room. The mop must not be stored with used cleaning solution. The textile and dirt deplete the germicide, and bacterial multiplication occurs. This results in painting the floor with bacteria. Mops used in the operating room must be laundered daily.

CONTACT LENSES FOR YOUNG CHILDREN

To the Editor:—*Are contact lenses recommended for treatment of simple myopia in teenagers or younger children? Is this age a contraindication?*

M.D., South Carolina.

Answer.—Until recent years, this consultant has been inclined to advise against contact lenses for children. More recently, with some refinements in contact lenses and with the increased recognition that social acceptance in the early teens is most important to children in this age group, this attitude has become more lenient. Contact lenses for children in their early teens may be prescribed under certain conditions. The corneal contact lens gives a better cosmetic effect and is tolerated better, but it offers less protection to the eye than does the scleral contact lens. The corneal contact lens is not adaptable for sports or swimming, while the scleral contact lens, which is not as good cosmetically, may serve an excellent purpose. Recently, it has been suggested (but without reasonable proof or confirmation) that contact lenses may have some influence on the course of simple myopia. This has yet to be corroborated.

HERPETIC LESION AND MENSTRUATION

To the Editor:—*What is the cause and treatment of mouth ulcers which begin about the time of ovulation and stop just before menses? They have been present since puberty in a 33-year-old woman. Her health otherwise has been normal since correction of a hypothyroid state with thyroid extract, and this treatment improved the mouth situation a little. The ulcers begin as small blebs. On alternate months they are worse—more of them and seemingly more inflammation secondarily. During two pregnancies there have been no ulcers, but they have returned immediately after delivery.*

Haywood L. Moore, M.D., Brunswick, Ga.

Answer.—Although ulcers of the mouth occurring before menstrual periods have been described for many years as recurrent or habitual herpes of the mouth, the herpetic etiology has not been definitely proved and, in fact, is denied by Blank and associates (Letter to the Editor, *J. A. M. A.* **142:**125 [Jan. 14] 1950) and by others. The distinction of herpetic lesions from etiologically different but similar types of recurrent stomatitis depends on the isolation of the virus and/or results of biopsy. Circulating antibodies to the herpetic virus are of importance more by their absence than by their presence and, indeed, are frequently absent in recurrent ulcers of the mouth. It has long been observed that the skin and mucous membranes are affected by the changing hormonal activities of the menstrual cycle. The mucosa of the oral cavity reflects these influences in a fashion similar to but not as demonstrable as that of the vaginal mucosa. Since the cause of recurrent ulcers is not known, aside from the definite but uncommon reaction to some foods, the one practical point of attack in this patient would seem to be on the menstrual cycle itself. The time relation here, after ovulation and when progesterone is greatest in amount, suggests that suppression of ovulation by estrogen therapy for a few cycles might be of benefit.

MENTAL RETARDATION

To the Editor:—*A 3-year-old girl does not yet speak, although otherwise she is apparently of normal intelligence. The parents are healthy, and pregnancy was normal. The patient, whose delivery record states, "cord around the neck of the baby," was born in asphyxia, and convulsions occurred during the first two days of life. When the patient was one day old, a lumbar puncture resulted in a normal-looking liquor (no gross hemorrhage). There was delay in her sitting up and walking, and now there is considerable delay in her starting to speak. She has now a vocabulary of 15-20 words (such as mommy and water), but she generally uses words which are not understood by the parents. Physical development, including hearing, is good, and the general intelligence is considered average. She started to use toilet facilities at the age of 2 years. Electroencephalographic study revealed beta waves generally of low amplitude and dysrythmia over the left hemisphere and no or minimal electric activity over the left parieto-occipital area. Some damage is demonstrable over the right occipital area as well. A neurologist who was consulted suggested small doses of x-ray therapy (4×100 r, to be repeated twice in two-month intervals). He claims to have seen good results in such cases. What is the prognosis of this condition? What therapy can be recommended? Is there any danger of further damage by a trial of x-ray therapy with the dosage indicated above?*

M.D., Washington, D. C.

Answer.—The cyanosis at birth and the early convulsions point to cerebral anoxia as responsible for the present mild mental retardation. The electroencephalogram as reported is of questionable significance. There would seem to be no rationale for

exposure of the brain to x-rays. The problem is one of education. Psychological evaluation in a year or two should be helpful.

NOCTURIA AND URGENCY

To the Editor:—*A patient, 80 years of age, has nocturia seven or eight times and spasmodic incontinence which is becoming almost chronic. About 1930, a median bar was cut, and a few years later a biopsy specimen was taken. He has no enlargement of his prostate and no residual urine, but he does have some stones in his prostate. He has, in addition, an asymptomatic stone in the lower calyx of the left kidney. In spite of all treatment, he still has to get up six or seven times at night, and sometimes his urgency reaches the point of incontinence. His nocturnal voidings seldom exceed 2.5 oz. At present, he is obliged to wear a urinal. He has used the routine preparations of hyoscyamus tincture and potassium citrate. Please give suggestions for further treatment.*

M.D., California.

Answer.—Presence of these symptoms and this history indicate that a complete urologic investigation should be performed, including calibration of the urethra and examination of urine specimens from each kidney. Urinalysis is of primary importance, since all of the patient's complaints could be due to infection alone. The capacity of the bladder should be carefully estimated. A small, contracted bladder may be the cause of such urgency and nocturia. If the bladder capacity is normal, the presence of prostatic obstruction must be suspected. Removal of the remaining obstructing prostatic tissue and the calculi might be beneficial. In view of the previous surgery, in the absence of infection and/or the presence of obstructing tissue in the posterior urethra, fibrous contracture of the vesical neck is a very likely possibility. This type of contracted vesical neck might be benefited by transurethral resection. Because of the age of the patient, nothing more radical should be done. Interference with an asymptomatic calyceal calculus is probably not warranted.

HEPATOLITHIASIS

To the Editor:—*What symptoms and findings may occur in a patient with a stone in the right or left hepatic duct or in one of its branches? Will jaundice occur with a stone in such a location?*

Seymour Levine, M.D., Jersey City, N. J.

Answer.—As long as calculi remain within the hepatic radicals, they seldom produce symptoms. The symptoms and physical findings are not considered diagnostic. Occasionally, because of the development of cholangitis and hepatic abscesses, patients may have fever and chills or other manifestations of acute inflammation within the liver. The main menace of intrahepatic calculi is their tendency to migrate into the extrahepatic bile ducts, with the production of biliary colic or obstructive jaundice. A stone within the right or left hepatic duct or in one of its branches should not cause jaundice unless there is extensive hepatic injury due to cholangitis or liver abscess. In most instances, hepatolithiasis is not recognized clinically until postoperative cholangiography is done. The surgeon should consider the possibility of intrahepatic calculi if the extrahepatic ducts contain small stones, biliary sand, or plugs of inspissated bile; if the hepatic bile is white or mucoid; if there are localized hepatic abscesses; and if intrahepatic calcified shadows are revealed by roentgenograms. Cholangiography is helpful in many instances in verifying the presence of and localizing intrahepatic stones.

HEAD-BANGING

To the Editor:—*A 2-year-old boy has been banging his head against his cradle and the wall for the last seven months. Apparently healthy, well-developed, and bright, he continues to do it, although the cradle has now been well padded, and even does it at night while asleep. He walks and talks. He has a sister now one year of age. He is not neglected and is given much love and affection. Is there any possibility of brain injury? How long does this habit usually continue?*

M.D., New York.

Answer.—Head-banging is a frequent manifestation of some degree of emotional disturbance, usually frustration or anger, though the psychodynamics are often more complex. It is more common in retarded children but by no means limited to them. The occurrence in this child, who is reportedly a normal child in all other respects and living in a healthy emotional environment, shortly after the birth of a sibling would make this the first etiological factor to investigate. It is impossible for the first born not to feel at least a quantitative lessening in attention with the arrival of the first sibling. The habit itself should be ignored while efforts are made to alleviate underlying emotional disturbances. This consultant is not aware of any instance where the head-banging has resulted in brain damage, although, from knowledge of the development of subdural hematoma after minimal trauma, the possibility exists. Make no effort to avoid the contusions that occasionally occur, as this may be an adequate object lesson to at least end the head-banging. The habit usually disappears before school age, but this will vary with the management of the etiological factors.

TREATMENT OF EXOPHTHALMIC GOITER IN CHILDREN

To the Editor:—*After subtotal thyroidectomy 18 months ago, a 14-year-old girl has had a recurrence of exophthalmic goiter on the right side of the neck. The recurrent lobe is much larger than the original thyroid gland, which weighed 62 Gm. The patient reacts well to thiouracil as far as her toxic symptoms are concerned; however, removal of the growth seems imperative. Should the patient be treated with sodium radioiodine, or is a thyroidectomy for the recurrent exophthalmic goiter preferable?*

C. A. Hellwig, M.D., Halstead, Kan.

Answer.—A conservative approach to treating exophthalmic goiter in children is desirable. In a recurrent exophthalmic goiter, the use of 300 mg. of propylthiouracil a day until the patient is in remission and 100 mg. a day as a maintenance dose for a period of two to three years should be employed. Inasmuch as the right lobe of the gland of this patient is enlarged, the size could possibly be controlled by administering concurrently either 2 grains (0.12 Gm.) of desiccated thyroid extract or 50 to 75 mcg. daily of sodium liothyronine in order to inhibit the overproduction of thyroid-stimulating hormone, which induces thyroid hyperplasia and increase in size of the gland. It is not advisable to use radioactive iodine in a patient this age because of the unknown long-term, undesirable possible carcinogenic effect. Subsequent resection carries the possibility of hypothyroidism or surgical complications, such as hypoparathyroidism. Long-term administration of propylthiouracil in a young patient who is periodically checked for drug reaction still offers the best opportunity.

SEDIMENTATION RATE DETERMINATION IN CHILDREN

To the Editor:—*What is the most accurate method of sedimentation rate determination in a 3-year-old child? What is the normal hematocrit value for a child of that age? With use of this hematocrit figure, is it valid to make the correction in the Wintrobe method, with the Wintrobe and Landsberg chart?*

M.D., California.

Answer.—The Westergren method is as accurate and as satisfactory as any test for the determination of sedimentation rate in a 3-year-old child. Micromethods are less accurate and also require more skill and experience. The micromethod of Landau requires special apparatus. The normal hematocrit reading for 3-year-old children, as recorded in literature, varies from 36 to 40%, according to the method used. The lower figures were obtained with dry anticoagulant agents which cause shrinkage of cells. Hematocrit readings of 38 to 40% in 3-year-old children are comparable to percentages of 48 for adult males and 43 for adult females. The Wintrobe and Landsberg correction chart was developed on the basis of a normal value for adult men of 47% and for women of 42%. It also takes into consideration the fact that a normal sedimentation rate in women is twice that of men, a condition which is not manifest in 3-year-old children. Hence, the chart is not applicable to children. The Westergren method is of such a nature that corrections for cell volume are not necessary.

THYROID MEDICATION FOR PATIENT WITH EPILEPSY

To the Editor:—*In a patient, aged 24, who has had epileptic seizures for 20 years and whose protein-bound iodine level is 2.8 mcg. per 100 cc., would thyroid medication be safe to use? Would the thyroid have any tendency to provoke or increase her seizures? The reason for thinking thyroid therapy could be indicated is irregular menstrual periods accompanied by premenstrual tension.*

A. L. Henrichsen, M.D., Van Nuys, Calif.

Answer.—It is safe to administer desiccated thyroid substance in the usual therapeutic doses to patients who have epileptic seizures. Thyroid substance does not have any tendency to provoke or increase the number of seizures which occur in epileptic patients. The indications for thyroid therapy in the epileptic patient are the same as those in any patient who does not have epilepsy. However, the decision as to whether a patient should or should not receive thyroid medication should not depend entirely on the values of protein-bound iodine in the serum. Although a level of 2.8 mcg. per 100 cc. of serum is low and usually does indicate hypothyroidism, the diagnosis should not rest on this one isolated finding. The patient's clinical appearance, the basal metabolic rate, and, perhaps, the result of the radioiodine uptake test should be considered before such a diagnosis is made. In female patients who have myxedema, the usual menstrual abnormality is an excessively heavy menstrual flow rather than irregular menstrual periods.

STEROIDS FOR EMPHYSEMA

To the Editor:—*A 56-year-old man has severe pulmonary emphysema and, with very little exertion, great difficulty in breathing. Have any of the steroids been proved to be of value in long-term therapy for this condition?*

Harold J. Grau, M.D., Rapid City, S. D.

Answer.—Corticosteroids often relieve symptoms of emphysema by reducing edema and spasm in the bronchioles. Many patients with emphysema are receiving such therapy. The dosage depends on trial, and one might start with eight tablets daily of any of these agents: cortisone, 25 mg., hydrocortisone, 20 mg., prednisone, 5 mg., or, preferably

(because of fewer side reactions), methylprednisolone, 4 mg., or triamcinolone, 4 mg. After several days the dose is gradually reduced and the smallest effective dose continued indefinitely with occasional rest periods to determine whether it is still needed. Other measures should not be neglected: prohibition of tobacco, bronchodilators, such as aerosols of adrenalin or isoproterenol, antibiotics for infection, digitalization for cor pulmonale, and, especially, perfection of diaphragmatic breathing. The patient taking corticosteroids should be observed for hypercortisonism, although this does not occur frequently with small doses and with the newer compounds.

TONSILLECTOMY AND STEROID MEDICATION

To the Editor:—*Is tonsillectomy contraindicated in a child who is taking steroid therapy for acute rheumatic fever if the sedimentation rate has returned to normal and if the child is operable in all other respects?*

J. J. Johnson Jr., M.D., Las Vegas, N. Mex.

Answer.—There is no contraindication to tonsillectomy in a child who has been receiving steroid therapy, within the circumstances stated. However, if the patient is still receiving steroid therapy, the preoperative preparation should be considered very carefully by an internist or pediatrician experienced in such problems. If the therapy has been stopped for three months or longer, a physician experienced in steroid therapy should evaluate the case as to whether preoperative preparation is necessary; if preoperative preparation is not given, he should be available for emergency treatment during and after the operation. This requirement should hold for a year after discontinuation of steroid therapy.

THE PINEAL BODY

To the Editor:—*Please give information regarding recent opinions on the pineal body. What is its function? Does it secrete a hormone? Is it a vestigial third eye?* *M.D., Canada.*

Answer.—Authorities are now generally agreed that the pineal body does not secrete a hormone. Tumors of the pineal body have often been found in association with sexual precocity, especially in males. It is thought, however, that these effects come about through pressure on the hypothalamic center and contiguous areas. There is no reference in any of the recent textbooks to a vestigial third eye.

APPEARANCE OF PHYSICIANS IN PUBLIC

To the Editor:—*The answer to the question concerning public appearance of physicians in* The Journal, *March 29, 1958, page 1666, is timely and enlightening. But please comment further on a specific aspect of the same question. Suppose a state university establishes, controls, and operates a noncommercial, educational television station and asks the faculties of its component colleges to produce popular programs in various fields of their competence. Would it be ethical for the university's college of medicine to participate in such an undertaking? Participation would involve members of the faculty appointed by the dean in a 30-minute weekly discussion on such subjects as health and disease, medical progress, and medical education. Medical subjects would be presented by full-time employees who do not maintain private offices and who accept as private patients only those persons referred by other physicians.* *M.D., Illinois.*

Answer.—The answer to this specific question is also contained in the answer to the original question. Even if the physicians participating did have a private practice, it would still be ethical for them to participate. The "Principles of Medical Ethics," published June, 1955, defines the duties of physicians to the public media of information in section 5 of chapter 1 in the following words: "The medical profession considers it ethical for a physician to meet the request of a component or constituent medical society to write, act, or speak for general readers or audiences. On the other hand, it may often happen that the representatives of popular news media are the first to perceive the adaptability of medical material for presentation to the public. In such a situation the physician may be asked to release to the public some information, exhibit, drawing, or photograph. Refusal to release this material may be considered a refusal to perform a public service, yet compliance may bring the charge of self-seeking or solicitation." With relation to the specific question now asked, the following paragraph from the same chapter is definitive: "An institution may use means, approved by the medical profession in its own locality, to inform the public of its address and the special class, if any, of patients accommodated." These "Principles of Medical Ethics" have been superseded by the shortened code, in which section 10 reads as follows: "The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual but also to society, where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and the well-being of the individual and the community." The only criticism this consultant has of the situation presented in the question is on grounds of showmanship rather than ethics. The kind of program envisioned would be fully as dull as it would be ethical.